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THE MONTH

ALTHOUGH the Ethiopian may not be able to change his skin, or the leopard his spots, the layman has still the fond hope that the doctor may be able to change his skin or remove his spots. All too often the doctor fails lamentably in supplying new skin for old, which is probably why our symposium on 'Diseases of the skin' is always one of the most popular symposia we publish. Although, unfortunately, unlike old soldiers, so many skin conditions do not fade away, the dermatologists are gradually bringing more conditions within the net of therapeutic control, if not cure. Perhaps the best example of this is tuberculosis of the skin, which is reviewed by Dr. Brian Russell. Iatrogenic disease is no prerogative of the dermatologist, but he is tending to see an increasing number of cases in which the skin lesion has either been caused, or exacerbated, by injudicious drug therapy. This is particularly applicable to the antibiotics, as pointed out by Dr. Mitchell-Heggs in his article on 'Antibiotics in dermatology', but the reader should also note Dr. Peterkin's warning in his article on 'The diagnosis and treatment of tinea pedis', that 'inappropriate treatment leads to a chronic disabling eczema'.

The Symposium

IF the *British Pharmacopœia* can be described as the pharmacist's bible, volume I of 'The Extra Pharmacopœia', the 24th edition of which has just been published (London: The Pharmaceutical Press, 1958. Price 65*s*.), can justifiably claim to be described as the doctor's bible. It is exactly 75 years since the first edition was published by W. H. Martindale, thereby ensuring, though probably quite unintentionally, that 'Martindale' should become perpetuated as a synonym for one of the classics of British medicine. The Pharmaceutical Society acquired the copyright in the 1930's. There could be no more striking commentary on the progress of therapeutics over the last three-quarters of a century than the fact that the first edition of 'Martindale' had 313 pages, whilst the new edition has 1695 pages. Even the last two decades have seen an increase of over 500 pages, for the 21st edition of 1936, the first to be published under the ægis of the Pharmaceutical Society, had only 1182 pages.

The Extra Pharmacopœia

The aim of the originator was to provide physicians and pharmacists with an epitome of information on the drugs used in Great Britain. This the new edition continues to do. There is a wealth of information concerning their use, supplemented with a selection of abstracts from recent articles. The

scope of the book can be judged from the fact that the section on cortisone and adrenocortical hormones occupies over fifty pages. There is no publication in which so much reliable information on such a wide range of drugs is collected together in such compact form. He is a foolish practitioner who deprives himself of the solace of having this book always on call in his consulting room.

A Spate of Specialties

'FACTS are chiels that winna ding' sang the Scottish bard. The following facts are culled from a recently published World Health Organization report on 'Medical Specialization' (London: H.M. Stationery Office. Price 1*s.* 9*d.*). Czechoslovakia leads the world in the number of recognized specialties—with 65. Among these 65 specialties are to be found balneology and oncology. Phoniatrics is a recognized specialty in France, whilst Poland recognizes community hygiene and hygiene of seafarers as specialties. In Denmark there are more specialists than non-specialists: 'in 1955, two-thirds of the physicians were specialists or had applied for specialist training'. In the United States, in 1954, of the 155,000 physicians in active practice, 65,000 were practising a specialty and 20,000 were 'interested in a specialty'. In the Union of South Africa a doctor cannot become a specialist until six years after qualifying, and he must submit proof that subsequent to qualifying he has spent at least two years in general practice or, in lieu thereof, has obtained other approved experience including at least one year in general medicine and/or general surgery. In the German Democratic Republic a physician must submit 'a *curriculum vitæ*, a police certificate of good character, a licence to practise, and evidence of his training and competence as a specialist' before he is allowed to sit the requisite examination to become a specialist.

Facts 'downa be disputed', according to Burns, but the implications of this spate of specialties give much food for thought. We in this country can indeed be thankful that we produce the best general practitioners in the world. If any additional evidence were required for the maintenance of the status of general practice it is this terrifying prospect of a world where health was dependent upon the unaided efforts of specialists.

Smoking in Cinemas

ACCORDING to a report in the April issue of the *NAPT Bulletin*, the Capital and Provincial News Theatres Ltd., London, decided to ban smoking in three of their cinemas on Mondays and Thursdays. After six months, however, the ban had to be discontinued as the three cinemas in question were acquiring the reputation of being permanently in the 'no smoking' category, and the decline in business was more marked than in the company's other cinemas.

This disappointing sequel to an experiment, upon which the company in question is to be congratulated, raises once again the question of why official action has not been taken to ban smoking in all cinemas and theatres. We are one of the few civilized countries which allow smoking in such

places. In France, Germany, the Netherlands, Scandinavia, Switzerland, and the United States, for instance, smoking is not allowed in cinemas. No-one wishes to impose more legislative 'don'ts' than necessary but, if smokers are not prepared to show consideration for that large section of the community (including many smokers) who do not wish to spend several hours in a pungent atmosphere of tobacco smoke, then authority must step in to retrieve the situation. If local authorities are not prepared to do what lies within their power to forbid smoking in cinemas and theatres, then it is up to the Ministry to take the requisite steps.

Altering Fingerprints

IT would appear as if a new hazard had been added to the life of the law-abiding dermatologist. Unless he is careful he may become the best friend of the fugitive from justice. At least, such is the dread prospect held out by J. W. Burke, Jr. (*A.M.A. Arch. Derm.*, 1958, **77,** 8) who throws out the suggestion that dermabrasion may be a means of circumventing that hitherto infallible means of identification—fingerprints. He gives details of two patients submitted to dermabrasion and reports that 'identification experts considered the post-planing fingerprints to be worthless in establishing the identity of the subject'. The patients themselves could detect no difference between their planed and unplaned fingers so far as appearance and reaction to heat and cold were concerned.

The beauty of this technique, from the point of view of the criminal, is that it leaves no tell-tale marks, so that there is nothing to arouse the suspicions of the examiner. Fortunately, however, for the peace of mind of the criminal investigation departments of the world, it is still possible for a skilled dermatologist to detect whether or not a finger has been planed. Even so, it looks as if the criminal has been able to put another spoke in the wheel of justice—even if only a small one. Will Scotland Yard now need to add a dermatologist to its staff to examine all fingerprint candidates in order to determine whether or not the fingers have been planed?

Children and their Pets

'THE biting of children by pets is a common, although rarely fatal, accident' and the child is more often at fault than the pet. Such are the two major conclusions of H. A. Carithers (*A.M.A. J. Dis. Child*, 1958, **95,** 150) as a result of a survey of mammalian bites of children. That the scope of the problem is by no means negligible is suggested by the fact that he estimates that in 1956 there were probably 25,000,000 dogs and 35,000,000 cats, in the United States, not to mention rabbits, squirrels, hamsters and rats which are also 'kept in great numbers by children'. A questionnaire submitted to 300 parents of 617 children coming under his care revealed that among the 531 children over one year of age, 15.4 per cent. had been bitten at some time by a mammal, 2.1 per cent. of them more than once.

Over a period of twenty months he saw 157 children who had been bitten

by mammals—the vast majority (132) by dogs. Boys were bitten more often than girls in a ratio of 3:2, and most of the children were between the ages of 2 and 10 years. Fifty of the children were bitten on the head, and only one on 'the traditional location, the buttocks'. It is with considerable regret that Carithers has to admit that the child was more often at fault than the pet. 'Quipsters prate', he says, 'that there are three American institutions above criticism—Motherhood, the United States Marines, and Dogs. We wish we could be the child's advocate rather than the dog's in the problem of bites, but, by a great majority in our series, the child, not the animal, was at fault'. The moral, of course, is obvious: that parents must accept full responsibility for training both child and pet. If there is one thing worse than depriving a child of a pet, it is omitting to train him to treat it with kindness and consideration.

The Val-de-Grâce

THE Val-de-Grâce Hospital, the French equivalent of the Royal Army Medical College and the Queen Alexandra Military Hospital, Millbank, was founded in 1793 by decree of the Revolutionary Convention, the premises being those of the monastery known as the 'Val-de-Grâce de Notre Dame de la Crèche'. The monastery, which dates back to the ninth century, has undergone many vicissitudes, but perhaps it reached its lowest level when the church, with its famous 131-feet high dome, was used as an anatomy theatre and military medical store following its desecration in 1793. Today the most interesting part of the Val-de-Grâce for the visitor is its military medical museum, of which Brigadier A. N. T. Meneces has recently given a description (*J. Roy. Army med. Cps*, 1958, **104**, 22) and which 'with its spacious halls and galleries, contains the finest available collection of documents, archives, models, relics, and souvenirs of military medicine'.

The archives, which are housed in the vaulted kitchens of the former monastery, contain the first commission granted to Larrey, the greatest military surgeon of his day, in 1792. One of the most interesting sections of the museum is that illustrating the development of means of evacuating casualties, which draws attention to the extent that the French have been pioneers in air evacuation. Over 160 cases were flown out from the siege of Paris by balloon in 1870, and the credit for being the first to transport a wounded man by air in the 1914-18 War is given to a French pilot, Captain Dancelzer, who flew a wounded Serbian airman to safety during the retreat of the Serbian army in 1915. The French army was also the first to introduce air ambulances—in Morocco in 1918. To the civilian, perhaps the most interesting exhibit is that dealing with the young French army medical officer, Ernest Duchesne, who, in 1897, submitted his thesis 'Contribution à l'Etude de l'Antagonisme entre les Moisissures et les Microbes' which demonstrated the prophylactic and therapeutic possibilities of penicillin.

BULLOUS ERUPTIONS OF THE SKIN

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During the last decade attention has been focused on the more obscure of the many disorders of the skin in which the development of bullæ is a prominent feature, mainly because of advances in knowledge of their differential pathology.

BLISTERS CAUSED BY EXTERNAL AGENTS

A host of chemical substances can provoke blisters on contact with the skin, due either to direct caustic action or to allergic sensitivity (fig. 1). The possibility that blisters may be provoked deliberately in this manner has to be borne in mind in certain circumstances. Dermatitis pratensis, a bullous eruption caused by contact with certain types of plant found in meadows and exposure to sunlight, is readily detected as a rule by the bizarre, often striated, arrangement of the blisters. Blisters can be provoked by insect bites and it may be difficult to differentiate between these and bullous papular urticaria.

INFECTIVE AND TRAUMATIC BLISTERS

Toxic causes.—Of these, drug eruptions are the most important. Potassium iodide is the best known, although bullous iodide eruptions are very rare. Other drugs which may provoke a bullous reaction more frequently are phenolphthalein, phenazone, the sulphonamides, the barbiturates and phenytoin.

Infective causes.—The primary blister of impetigo contagiosa is usually small but may vary a good deal in size, especially in children. The blister of epidemic impetigo of the newly born (pemphigus neonatorum) is usually large and filled with clear fluid. It can usually be cured without great difficulty and is no longer regarded as a dangerous infection.

The serious bullous virus infections, generalized herpes and generalized vaccinia, occur almost exclusively in infants and children suffering from the eczema-asthma syndrome. For this reason vaccination is strongly contra-indicated in these cases.

CONGENITAL TRAUMATIC BULLOUS DYSTROPHIES

Epidermolysis bullosa.—The cases are usually divided into two categories—simple and dystrophic—according to the severity of the process. In the former blisters appear only at the sites of trauma; in the latter they occur also on parts not obviously subjected to trauma and in the mucosæ. The nails are involved, becoming atrophic in the long run. The most severe form (epidermolysis bullosa letalis) is fatal during the first or second year. The simple type is genetically dominant; the dystrophic, which is incompatible

with a normal expectation of life, is recessive. In both types, after healing, blisters leave scars some of which contain small epidermal cysts (milia) (fig. 2). The simple type usually improves or ceases in adolescence.

Acquired epidermolysis bullosa.—The rare cases which develop in adult life do not differ clinically from the congenital disease.

Cockayne type.—Blisters occur exclusively on the feet, especially in the interdigital clefts and on the soles. They are associated with hyperidrosis and the blisters appear usually only in hot weather. Genetically it is strongly dominant.

FIG. 1.—Bullous eruption caused by contact with parsnips.

Dowling and Meara (1954) described a bullous dermatosis under the heading, epidermolysis bullosa, resembling juvenile dermatitis herpetiformis, and without doubt it is often regarded as the latter. It begins in the first few weeks of life and resembles the dystrophic form of epidermolysis bullosa in that blisters develop both as the result of trauma and spontaneously in parts not obviously subjected to trauma. In severe cases the mucous membrane of the mouth may be involved. Scarring and epidermal cysts are not seen. A characteristic feature is the development of dense hyperkeratosis of the palms and soles (fig. 3), especially the latter, which follows repeated blistering. In the cases observed the family histories have been negative.

FIG. 2.—Epidermolysis bullosa dystrophica (milia).

BULLOUS ERUPTIONS DUE TO SUNLIGHT

In addition to the bullous reaction of normal subjects which may follow overexposure to sunlight or to extreme cold, there are a few rare diseases in which this reaction to sunlight is excited by normal exposure. The most important is the rare inborn error in erythropoiesis in which porphyrins in abnormal amount are found intermittently or continuously in the serum, urine and fæces. First fully described by M'Call Anderson (1888) as *hydroa æstivalis* with porphyrinuria, the term porphyria is employed alone for this disease in

modern terminology, and the cases are divided into congenital, acute and late chronic porphyria.

Of these the *congenital cases* are the most rare. Blisters occur from early childhood on the exposed parts in the spring and summer and in the course of years may lead to severe scarring and mutilation. Porphyrin is deposited in the teeth, giving rise to a pink discoloration, and in the bones. Very rarely, porphyria has been associated with hæmolytic anæmia which, in some instances, has ceased after splenectomy. In the *acute* type, intermittent episodes of serious gastro-intestinal, neurological and mental symptoms occur and the disease may be fatal. Hydroa does not occur.

FIG. 3.—Epidermolysis bullosa.—Recurrent blistering and hyperkeratosis of the soles.

Chronic late porphyria resembles congenital porphyria in its cutaneous manifestations although the degree of scarring and mutilation is less severe. Abdominal cramps or colic occur exceptionally. The condition is familial and probably represents a late development of the congenital disease (Brunsting and Mason, 1949; Wells and Rimington, 1953). Liver damage, often produced by chronic alcoholism, appears to be a contributory factor. Wells and Rimington have demonstrated the presence of porphyrins in abnormal quantity in the bile, and that the site of action of light was probably on the capillary walls of the uppermost part of the dermis. In chronic porphyria whether congenital or late, the skin which has suffered damage from sunlight is also sensitive to trauma, and the reaction to trauma, blistering and subsequent scarring with milium bodies, simulates that of epidermolysis bullosa, to which, however, the disease is unrelated.

In *hydroa vacciniformis*, first described by Bazin and later by Hutchinson under the heading of *recurrent summer eruption*, the lesions are primarily small blisters which enlarge, become filled with pus, umbilicate and ultimately heal to leave scars like those of smallpox. The disease begins in early life and only the parts exposed to sunlight are involved. Whether or not this extremely rare disease, of which I have seen but one example, in which no porphyrins could be found in the urine or fæces, is related to M'Call Anderson's disease is uncertain.

BULLOUS ERYTHEMA MULTIFORME

The characteristic symmetrical distribution of the lesions, their target-like

configuration and the short self-limited course, will usually serve to differentiate this from other bullous eruptions, although the characteristic disposition of the lesions on the hands, fingers, wrists, elbows and other prominences is not quite constant. Whether the Stevens-Johnson syndrome

FIG. 4.—Dermatitis herpetiformis.

FIG. 5.—Very characteristic appearance of well-established case of dermatitis herpetiformis. Some small flat bullæ will be present in the polymorphous eruption.

ought to be regarded simply as a severe form of bullous erythema multiforme is not settled. Blisters develop predominantly in the mouth, whilst the cutaneous eruption is characteristic of bullous erythema multiforme. It occurs predominantly on the face and in the genito-crural area, but there are additional blisters of widespread distribution. Urethritis and conjunctivitis commonly accompany the eruption. The attack is febrile and the patient may be seriously ill during the efflorescent phase which lasts for ten to fourteen days.

DERMATITIS HERPETIFORMIS (DUHRING'S DISEASE)

It is customary in this country to restrict the use of this term to a well-defined and not very rare disorder. Its elements are polymorphic, consisting of patches resembling urticaria or erythema multiforme, but essentially bullæ of variable size, often quite small and not obvious without close inspection. Itching is severe and persistent but the health of the patient is not otherwise disturbed. In the course of months or years the polymorphic appearance of the eruption is increased by pigmentation and small super-

ficial scars. The distribution is highly characteristic, the eruption being disposed mainly on convex surfaces: the scalp, the shoulders, the posterior aspect of the elbows (fig. 4) and the neighbouring part of tha upper limbs, the buttocks (fig. 5) and lumbo-sacral area. The genito-crural area is also attacked with some frequency. The disease persists indefinitely although its spontaneous disappearance after some years has been observed occasionally in adults and much more often in children. The cause is unknown.

FIG. 6.—Bullous pemphigoid.

PEMPHIGOID

The French include this condition under the general heading *dermatite polymorphe douloureuse* or Duhring-Brocq disease. It differs very considerably, however, in its morphology, its distribution and its behaviour from classical dermatitis herpetiformis, and in this country and in America the term pemphigoid is usually preferred. The age incidence is generally later than that of dermatitis herpetiformis of which some think it may be a senile variant, but classical dermatitis herpetiformis is also met with in the very old. The arguments in favour of differentiating pemphigoid from both dermatitis herpetiformis and pemphigus have been well set forth by Prakken and Woerdeman (1955) who suggest the name parapemphigus.

The eruption consists essentially of rather large tense bullæ (fig. 6), some of which may contain blood, and occasionally some patches of gyrate or circinate erythema. The blisters are commonly somewhat restricted in distribution for a while but eventually they become widespread. Itching may be rather pronounced but it does not appear to be as intense as in dermatitis herpetiformis. Pemphigoid is a far more serious illness than dermatitis herpetiformis, but the incidence of spontaneous cure is higher.

In one series of 38 cases (Rook and Waddington, 1953), eight cleared up in periods varying from three weeks to 5½ years. Twelve of the same series died after an average duration of 14½ months, mainly from intercurrent illness.

Bullæ complicating eczema.—Blisters of the pemphigoid type are occasionally seen during the course of more or less severe eczema, most often on the legs, and this development may suggest the alarming possibility that an additional process has been superimposed. The bullous complication subsides fairly readily, however, when the eczema has been brought under control and it evidently has no independent existence.

HERPES GESTATIONIS

This rare disease appears in the first or a subsequent pregnancy, usually

from the fourth or fifth month onwards. It clears up usually within about a month of parturition and reappears in subsequent pregnancies, either regularly or intermittently. Small recurrences sometimes occur at the menstrual periods for some months. The subject has been studied and reviewed recently by Russell and Thorne (1957), who had the opportunity of observing three cases within a short period. They point out that the eruption bears no close resemblance to that of classical dermatitis herpetiformis but rather more closely resembles pemphigoid, particularly cases in which polymorphic erythematous lesions are found together with blisters. They also point out that the same type of eruption has been observed in a case of chorio-carcinoma (Elliott, 1938) and in one of hydatidiform mole (Tillman, 1950). They express no opinion regarding the precise etiology of the condition.

BENIGN MUCOUS MEMBRANE PEMPHIGOID

This is a new name for the disease which for a great many years has been known as ocular pemphigus. The subject has been well reviewed and studied on the basis of seven cases by Church and Sneddon (1953). According to these authors the disease usually begins with mucosal lesions, and these may be present for years before the eyes become involved. They are seen commonly as superficial, relatively painless erosions on the buccal mucosa which leave white scarring. The nasopharynx, uvula and œsophagus may also be involved. Similar lesions are met with on the genitalia of both sexes.

In rather less than half the cases one or a small number of skin lesions occur in the form of bullæ recurring *in situ* over a very long period. These may precede both mucosal and ocular changes by a number of years. They cause scarring and the lesion is seen often as a reddened scarred plaque with peripheral blisters. The scalp and face are involved more often than other parts but no part is exempt. In the conjunctivæ the disease begins as a simple catarrhal conjunctivitis; in due course this is followed by the development of scar tissue, shrinkage and adhesions between the palpebral conjunctiva and the limbus. In the final stage the lids become fixed to the globe, restricting movement. Xerosis, corneal ulcers and perforation may follow.

PEMPHIGUS

The essential lesion of dermatitis herpetiformis, pemphigoid, herpes gestationis and benign mucous membrane pemphigoid, is a blister which develops beneath an intact epidermis. In fact, histologists can say no more about these blisters than that they are of the dermatitis herpetiformis type. The blisters of pemphigus are altogether different, a fact which was made abundantly clear by Dupont and Piérard (1938, 1949), Civatte (1943), and Tzanck (1948). The blister of pemphigus is intra-epidermal (fig. 7) and its site appears to determine the clinical type of pemphigus. If the epidermal cleavage is very superficial—subcorneal—the effect will be pemphigus foliaceus; if deeper, bullous pemphigus, generally called pem-

phigus vulgaris, will result, or perhaps pemphigus vegetans. The process of cleavage of the epidermal cella is known as 'acantholysis'.

The malpighian cells are deprived in some way of their intercellular fibrils and become dissociated from one another. In the fluid of a blister altered malpighian cells, round with large nuclei (fig. 8), rather clear surrounding cytoplasm and a more darkly staining border can be seen near the edge of the split. These cells can be seen also in the stained scraping of the floor of a blister. The cause of the process is unknown.

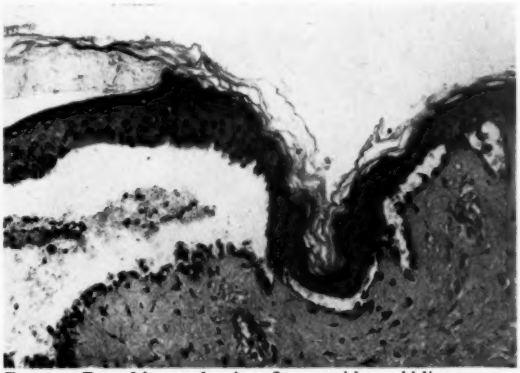

FIG. 7.—Pemphigus vulgaris.—Intra-epidermal blisters containing acantholytic cells.

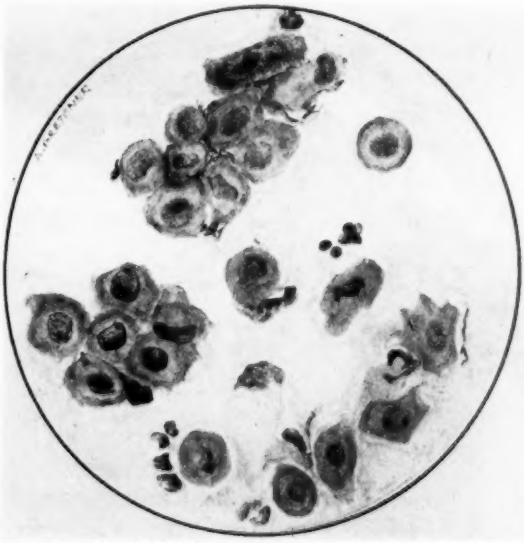

FIG. 8.—Blister fluid from pemphigus, showing acantholytic cells (clumped and single).

Pemphigus is a malignant disease from which complete recovery can hardly be expected, although since the advent of treatment with corticosteroids, long remissions have been observed.

CLINICAL TYPES OF PEMPHIGUS

Pemphigus erythematodes (*Senear-Usher syndrome*).—The onset is insidious in the form of rather moist scaly areas most often on the face, chest and back (fig. 9), resembling those of seborrhœic eczema. It is usually possible to detect small flaccid bullæ in the borders of some of the patches and the diagnosis is generally not long in doubt. The disease may remain stationary for a long period, even several years, but subsequently it will develop into one of the forms of the generalized disease, most often pemphigus foliaceus but occasionally pemphigus vulgaris.

Pemphigus foliaceus.—In the fully developed disease there is universal desquamation (fig. 10), in which small flaccid bullæ (fig. 11) can always be detected in places, the process being one of continuous detachment of small fragments of horny epidermis by underlying blisters. The evolution is exceedingly slow and the general health is moderately well maintaned, perhaps for some years. Sooner or later the patient becomes cachectic and dies, often from intercurrent infection. Intractable diarrhœa may be a distressing terminal symptom.

FIG. 9.—Pemphigus erythematodes.

Pemphigus vulgaris.—The acantholytic cleavage is situated at a greater depth than in pemphigus foliaceus. Blisters develop in any region, and sometimes primarily in the mucosæ, rarely in the conjunctiva, although the disease has nothing to do with 'ocular pemphigus'. They may be localized to a single area for a long while and generally the evolution of pemphigus is slower than that of pemphigoid with which it may be readily confused on clinical grounds. Eventually blisters become widely distributed over the surface. They appear on apparently normal skin but if this is subjected to vigorous friction the most superficial layer is found to be readily detached from the deeper part of the epidermis (Nicolsky's sign). If untreated the evolution of the disease is inexorably towards death in two or three years in progressive toxæmia and cachexia, or from intercurrent infection. Reports of spontaneous cure may be questioned, the differential diagnosis from the more benign pemphigoid having been difficult before the establishment of absolute histological diagnostic criteria.

Pemphigus vegetans.—The initial lesion is a blister like that of pemphigus vulgaris, but there is a predilection for the large and small folds, the axillæ, genito-crural areas, umbilicus and the corners of the mouth. The mucous surfaces may be affected. On the eroded surface of the primary blisters, papillomatous vegetations develop and confluence of these vegetations form large moist plaques. There is a tendency towards spontaneous temporary remissions and on the whole it pursues a more indolent course than pemphigus vulgaris. Vegetations may also develop in the folds during the course of pemphigus vulgaris.

TREATMENT

Dermatitis herpetiformis.—At one time it was possible to relieve the intense itching of dermatitis herpetiformis only with arsenic given by mouth, usually

as Fowler's solution. This was a thoroughly unsatisfactory treatment because in many of the cases chronic arsenical poisoning developed sooner or later in the form of arsenical pigmentation, keratoses, peripheral neuritis and, in the course of years, multiple basal cell or intra-epidermal carcinoma of the skin. Sulphapyridine was a welcome substitute but this also is a somewhat unpleasant remedy which not every patient is able to tolerate, especially when it is necessary to exceed the dose of 2 g. daily.

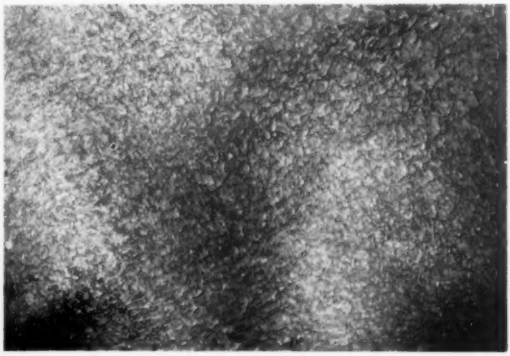

FIG. 10.—Pemphigus foliaceus, fully developed.

Finally, Kruizinga and Hamminga (1953) introduced diaminodiphenyl-sulphone (dapsone), and this has proved to be a striking advance. The dose of 100 mg. daily, which is usually well tolerated in the long-term treatment of leprosy, is adequate for the suppression of symptoms in the majority of cases of dermatitis herpetiformis, and even a somewhat smaller dose may suffice. Its side-effects—cyanosis and normocytic anæmia—are usually overcome spontaneously within a few months without withdrawal of the drug or reduction in dosage. Children may not tolerate the drug as well as adults. Dapsone may be ineffective in exceptionally widespread cases.

FIG. 11.—Pemphigus foliaceus, early stage.

Pemphigoid.—This condition does not usually respond at all to dapsone, sulphapyridine or arsenic, but it can almost always be brought under control with the corticosteroids and this at present appears to be the appropriate treatment in the great majority of cases. The dose required varies greatly but it is usually high. It may be determined either by stepping up gradually until the blisters are brought under control, or a large daily dose may be given from the beginning. In either case the initial suppressive dose is

stepped down gradually until the lowest controlling dose is reached, and this may be quite low. In a proportion of cases blisters cease to appear after a few to several months and the treatment may then be stopped altogether. The initial suppressive dose is often of the order of 400 to 500 mg. of cortisone daily, or about 80 mg. of prednisone.

Pemphigus.—The suppressive dose of cortisone required for the treatment of pemphigus is usually higher than in pemphigoid, as much as 1 g. daily being required in some cases, but it can be stepped down as in the treatment of pemphigoid and in a proportion of cases remissions have followed during which no treatment is required. The less malignant forms of pemphigus, pemphigus foliaceus and pemphigus vegetans, may require a somewhat smaller initial suppressive and final maintenance dose. Opinions differ regarding the treatment of the most benign form of all, pemphigus erythematodes, for this form may require rather heavy dosage which might reasonably be considered to be unjustifiable in the circumstances. The better policy may be to withhold treatment until the disease has developed more fully and the symptoms have become intolerable. Owing to the large dosage required for the treatment of both pemphigus and pemphigoid, serious side-effects are commonly encountered, particularly diabetes mellitus and bone decalcification.

It is impossible to say whether the ultimate mortality rate of the two diseases has been altered by the treatment, but in many cases life has certainly been made far more tolerable and even prolonged.

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ROSACEA

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UNTIL the middle of the last century rosacea was regarded as a variety of acne vulgaris. Then, in 1842, Erasmus Wilson suggested that acne should be divided into two sections: acne simplex (i.e. acne vulgaris) and acne rosacea. This suggestion was widely accepted and seems to have remained unquestioned until the nineteen-twenties when in the British Isles—possibly more by tacit agreement than by controversy—the word acne was dropped and the term rosacea retained. The alteration was sensible: Plumbe (1837) had defined acne as 'obstruction or simple inflammation of the cutaneous follicles', and rosacea is not a malady in which the follicles are primarily concerned.

THE PATIENT AND HER HISTORY

The patient is usually a woman some thirty or forty years of age who complains of redness of the face; by this she means a persistent vasodilatation of the central areas of the face which is manifest as an increase in the depth of skin colour. Often, as Wittkower and Russell (1953) observed, she sits on the edge of her chair, a neatly but unassumingly dressed woman who clutches her handbag tightly on her lap. She is shy, somewhat apprehensive, and quiet, but if her confidence is gained she may become less reserved. If asked a question which she regards as pertinent a flush may increase the colour of her face. Sometimes she will agree that the malady developed slowly and insidiously, but in some cases it may have developed rapidly. The classical story is that at first there was simply a temporary flushing during and after meals, after exposure to changes of temperature and sometimes at the 'periods'. In a few cases—in answer to a direct question—she may report that she has noted gustatory sweating (though this is rare and, when noted, is more often in men than women). She will add that when this flushing had continued unrelieved for some time, the face became permanently red and many small blood vessels became noticeable. The erythema is limited to the nose, the adjacent parts of the cheeks, the chin and the middle of the forehead. In severe cases nearly the whole of the cheeks may be involved, and the invasion of the forehead is not limited to the central area (fig. 1, 2). The borders of the erythematous areas are not sharply defined, and the vascularity can be obliterated by pressure.

Radcliffe Crocker, who described all this accurately in 1888, noted that in spite of its fiery redness the nose is often colder than normal to the touch. The malady may not progress further but more often, after a variable time (usually months or years but sometimes simultaneously with the permanent vasodilatation), papules, pustules and small nodules develop. Crocker and his contemporaries regarded the transitory flushings as the first stage of the

disease and the permanent flush as the second stage; this is a reasonable division. In the majority of cases, although there are fluctuations, there is no material cutaneous increase of the malady beyond stage two, but there may be ocular involvement. In a minority of cases (many more in men than in women) rhinophyma may develop (fig. 3), and this constitutes the third stage of rosacea. Rhinophyma, however, may develop without flushing of the face and nose and be the sole evidence of the rosaceous complex (Beerman, 1956). In a few cases spontaneous remission may occur at any time in the first or second stages. The patients do not complain of pain or tenderness or burning of the skin, but they may complain of soreness of the eyes, for, as Doggart (1957) has noted, they are liable to blepharitis, conjunctivitis, Meibomian cysts and—much less often—to vascular corneal keratosis, the last being the only specifically rosaceous condition.

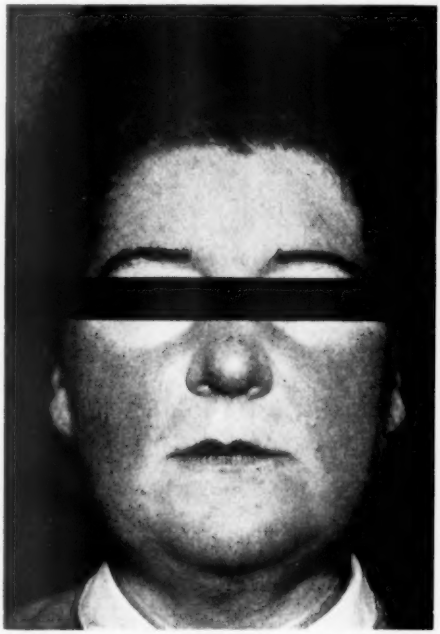

FIG. 1.—Somewhat extensive rosacea in the second stage.

In many cases, the patient's tongue, which will be protruded slowly, is smooth and has a diffuse whitish coat over its whole surface: the anterior edge is rounded: the lateral edges are often depressed below the flat plane of the superior surface. The organ contrasts markedly with the red, pointed, viperine tongue which in some other maladies is rapidly flicked out of the mouth and quickly withdrawn. Not infrequently patients with rosacea have symptoms of mild flatulent dyspepsia, but seldom mention these unless asked.

DIFFERENTIAL DIAGNOSIS

Usually the diagnosis is easy. Few of us confuse seborrhœic dermatitis, eczema or lupus erythematosus with rosacea, for these are conditions which, if one thinks for a moment, are quite different in appearance. Nowadays we need scarcely give a thought to the rarer manifestations of syphilis or lupus vulgaris, but I have known a very few cases in which a halogen rash due to iodides was mistaken for rosacea. The most important 'snag' is not to miss cyanosis due to heart disease; the diagnosis here depends more upon adequate

examination of the patient than on mere inspection of the facial congestion. There is, however, one differential diagnosis which may be extremely difficult; Lewandowsky (1917) described a rosacea-like tuberculide, and there must be very few skin clinics where from time to time the question 'is this "a Lewandowsky" or a rosacea?' has not been asked. This tuberculide is characterized by an eruption on the face of small, discrete, dusky red, persistent papules often associated with a reddish congestion; but the papules are said not to develop on the nose and they do not become pustular. Ingram and Brain (1957) state that if the papules are examined by diascopy (i.e. under the pressure of a suitable piece of glass) faint, brownish yellow, central puncta looking like apple-jelly nodules may be seen. Biopsy may assist diagnosis, but even an expert histopathologist may find differential diagnosis difficult. Fortunately, Lewandowsky's tuberculide is a rare complaint whilst rosacea is common.

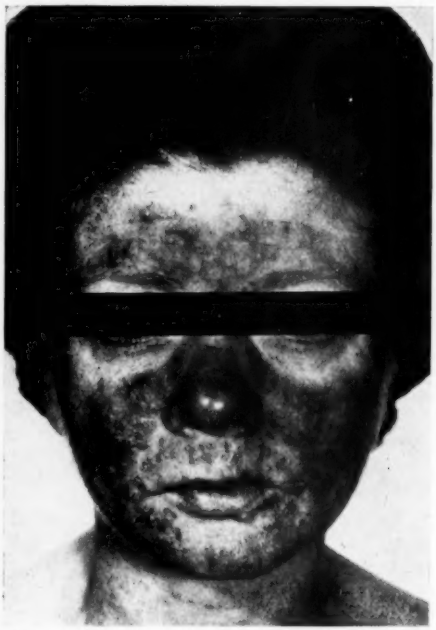

FIG. 2.—Severe rosacea in the second stage, showing papules and pustules.

BASIC DATA

The malady is fairly common and there must be few general practices in which cases could not readily be found. Crocker, who was in charge of the skin department at University College Hospital, reported an incidence of 'more than 2 per cent. of all cases' in his clinic. In 1956 and 1957, at St. Bartholomew's Hospital the incidence was 1.1 per cent. of new cases. Females preponderate, but possibly there has been some change in the relative incidence, for Crocker reported a ratio of 5 females to 1 male but noted that the difference diminished after forty years of age.

Borrie (1953) analysed 130 uncomplicated cases of rosacea at St. Bartholomew's and Barnet General Hospitals and found the incidence to be 2.5 females to 1 male, but when the cases were divided into age-groups, between the ages of 40 and 49 years the ratio was 27 men to 26 women and in the next decade 13.5 men to 8.6 women. Wiener (1955) states that the sex ratio is 3 females to 1 male in North America and Denmark and 3.2 in South America.

There is an old argument (e.g. Stelwagon, 1904) as to the validity of these

figures, because women probably demand treatment for a facial disfigurement more readily than men; when Borrie analysed a series of 99 cases suffering from ocular and cutaneous rosacea conditions which, because of the painfulness of the eyes, forced patients to seek treatment—the sex incidence was 1.3 females to 1 male. Familial rosacea has been reported, but is rare; the evidence studied by Wiener suggests that familial rosacea tends to become manifest relatively early in life.

Whilst many are taught that rosacea often begins at the menopause, Crocker emphasized that 'the age of onset is over twenty-five years, beginning in fact at the age when acne vulgaris is ceasing to appear'.

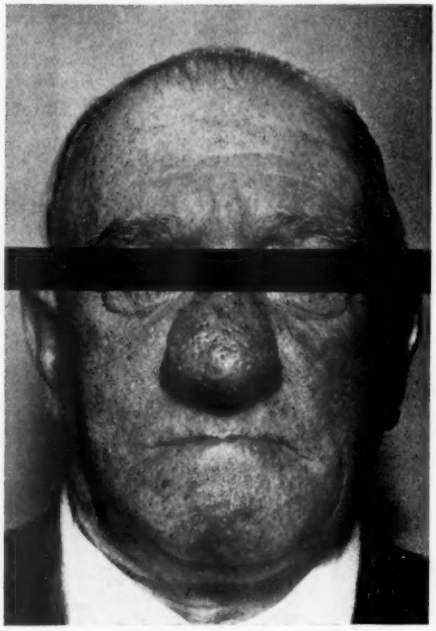

FIG. 3.—Rhinophyma.

Stokes and Beerman (1932) found that in 68 of 83 patients the average age at the onset of the malady was 32.1 years, but in one case it appeared in childhood (10 years) and in another in old age (68 years). In two-thirds of the cases the onset was slow: in the remainder it was rapid but not explosive. In Borrie's analysis the highest incidence of onset in both sexes was between 20 and 49 years of age but, whilst more women developed rosacea between the ages of 30 and 40 years than at any other time, as many men (27 per cent.) were first afflicted between the ages of 30 and 39 years as between 40 and 49 years.

According to Eastwood (1928), the association of ocular lesions with rosacea was originally described by Arlt (1864) who referred briefly to involvement of the conjunctivæ and corneæ.

In Borrie's analysis, of 99 cases suffering from ocular and cutaneous rosacea, 80 per cent. of the women first suffered from ocular involvement between the ages of 30 and 59 years: in men 25.6 per cent. suffered this involvement between the ages of 20 and 29 and 65.1 per cent. between 30 and 59 years. In 53 per cent. of his cases rosacea first appeared on the skin before the eyes were involved: he noted that cutaneous manifestations of rosacea could precede ocular ones by anything up to 30 years, or vice versa. Ocular lesions are more common in men.

The duration of the malady reflects the ineffectiveness of treatment. Borrie noted that 17.2 per cent. of women when first seen had had the malady for six to ten years; the figure for men was 18.8 per cent. for a similar period. He noted individual cases which had persisted for periods of 15 to 43 years.

HISTO-PATHOLOGY

So far as is known, the cutaneous primary pathological abnormality in cutaneous rosacea is dilatation of the most superficial vessels in the skin, which are non-muscular endothelial capillaries and venules. Telangiectasia occurs when the contractile power of these vessels is overcome.

Borrie has shown that, whilst the deeper muscular vessels (arterioles) are more dilated when at rest and possess a greater potential for further dilatation than normal, they can contract or dilate without affecting the intensity of the rosacea. There is a varying degree of inflammatory reaction about the dermal appendages consisting chiefly of lymphocytes with some histiocytes and plasma cells. Some destruction of the sebaceous glands occurs, and there is subsequent fibrosis (Ormsby and Montgomery, 1954). Lever (1954) states that in a significant number of patients foci of epithelioid and Langerhans giant cells may be seen and then the differential diagnosis from cutaneous tuberculosis is difficult. In rhinophyma the sebaceous glands are increased in size and number: their orifices are dilated and filled with keratin and sebum: peri-folliculitis and intra-follicular abscesses may be observed: there is hypertrophy of the connective tissue, and dilatation of the blood vessels which are surrounded by a chronic inflammatory infiltrate.

ETIOLOGY

The major problem is why the endothelial capillaries and venules dilate and become telangiectatic. At the outset it must be stated that no-one has yet found the answer.

Because even the least observant of patients noted that in the early stage the flushing of the face was associated with the ingestion of food, for long it was believed that rosacea was a manifestation of some defect in gastric digestion. Originally this defect was attributed to an excessive ingestion of alcohol: nowadays in the majority of cases an excessive intake of tea and coffee associated with a great partiality for carbohydrates is much more often responsible. Seventy years ago Crocker (1888) wrote that tea and coffee were often, but not necessarily, injurious, and beer, stout and acid wines particularly noxious: digestible food, he said, should be chosen and he recommended alkalis and carminatives for cases in which there were signs of irritative dyspepsia, and mineral acids if atony of the stomach was suspected. When he wrote this advice Crocker had never seen an x-ray photograph of the stomach or a report of a fractional test meal, but *faut-de-mieux* one has often given the same advice. There is, in fact, very little evidence that rosacea is a gastric malady with cutaneous manifestations, yet in many cases with gastric symptoms the rosacea is relieved by appropriate treatment on the lines which Crocker advocated.

Ramel (1939) suggested that certain substances ingested as food escape digestion and are absorbed in a form which gives them the power of vasodilatation. Usher and Young (1956) made gastroscopic studies and found that in eight patients with rosacea, all showed evidence of gastritis. Gastroscopy was reported in four of these cases when the rosacea had improved, and in each a normal gastric mucosa was then revealed. They suggest that rosacea is a general vascular disturbance with presenting signs on the face, but—as yet—there seem to be no confirmatory publications concerning their findings. Some have considered that rosacea is due to deficiency of riboflavine: this view has had many advocates and many opponents (Beerman, 1956).

In contrast to what may be called the 'internal etiology' of rosacea are

the suggestions of Ayres (1949), Ayres and Anderson (1932) and Søbye (1950). Ayres believes that in some cases the cutaneous parasite, *Demodex folliculorum* (fig. 4), is the cause of the malady. One presumes that there is a little evidence to support this view in the fact that the use of simple lotions, e.g. calamine with sulphur or ichthammol, or sulphur lotion, confer benefit in some cases, but so little is known of *Demodex* and the applications which may affect its activities that one would not like to press this argument.

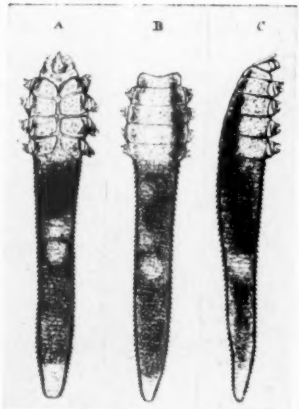

FIG. 4.—*Demodex folliculorum*. An early engraving from Erasmus Wilson's book (1842).

Haxthausen (1919, 1930, 1932) pointed out that hyperæmia and telangiectasia with degeneration of cutaneous elastic tissue were characteristic of damage caused by light and concluded that the combined effects of cold and light were prime factors in the etiology of rosacea. One argument which would be submitted against this hypothesis is that in a majority of cases the patients seem to be persons who have not had much exposure to wind and weather: but these factors should not be lightly dismissed. Søbye, whose iconoclastic views considerably disturbed the tranquillity of dermatological thought in 1950, postulated that the continual actions of light, cold and heat were major etiological factors in predisposed persons.

In regard to the deleterious effect of light, he suggested that because the submental area is always (*sic*) spared in cases of chronic, polymorphous actinic eruption, but may be affected in rosacea, exposure to light is not always the cause of rosacea. He postulated that in predisposed individuals climatic agents cause injury to the small vessels of the face at the sites of predilection; this causes œdema which is not removed from the areas if the facial muscles are not continually in motion. In time the œdema leads to metabolic difficulties, the products necessary for anabolism being delayed in reaching the skin and the products of catabolism being slowly removed. Infiltration and fibrosis may thus develop.

Focal sepsis has often been inculpated (e.g. Hellier, 1939), but critical studies have often failed to correlate infection with the rosacea (Beerman, 1956). The possibility that rosacea may be due to some neurological abnormality causing vasodilatation of the facial blood vessels must often have been considered but no great advance has been made along this path, attractive though it is. Even Søbye (1950) has to admit that in about 20 per cent. of his cases he could not exclude the possibility that seborrhœa may influence the picture; but seborrhœa (meaning overactivity of the sebaceous glands) is not a marked feature in most cases of rosacea. Nevertheless, acne vulgaris may merge into rosacea: Stokes and Beerman (1932) noted that 58 per cent. of their rosacea cases had, or had had, acne vulgaris, whilst 'distinct seborrhœic processes other than acne' were noted in 48.1 per cent.

The seborrhœic state, which probably implies an abnormality in cutaneous sugar metabolism, and perhaps defects in the liver and other organs, and perhaps also in the endocrine system, cannot be disregarded as a factor in the etiology. There is a tendency at present to disregard gynæcological factors as being of major etiological importance in women suffering from rosacea. Both Søbye (1950) and Wise (1943) failed to correlate rosacea with menstrual abnormalities and the former found no correlation between the malady and diseases of the ovaries and uterus, but he thought that the menopause did 'play a certain part' in some cases.

Finally, there is much evidence that emotional factors are of importance in the evolution and persistence of the malady.

Stokes and Beerman (1932), Klaber and Wittkower (1939), Cormia (1950), Wittkower and Russell (1953), and Obermayer (1955) have all drawn attention to these matters. Wittkower and Russell accept the observation of Wingate Todd and his colleagues (1928-29, 1930) that anxiety diminishes gastric tone and inhibits peristalsis; they think it probable that when the stomach provokes rosacea, motor rather than secretory changes are responsible (e.g. Wittkower, 1935). They suggest that emotional changes may cause a permanent blush by direct action on the vessels of the face, but—perhaps more often—these changes act by lowering gastric tone and thus cause the erythema of the face. Beerman (1956) seems to be somewhat sceptical of generalizations concerning the psychodynamics of rosacea and suggests that 'further study of patients, individually as suggested by Macalpine (1954), may eventually elucidate the true place of psychosomatic factors in rosacea'.

TREATMENT

In view of the multiplicity of views concerning the etiology of the malady, it is extremely difficult to discuss treatment. At the outset it is best to take the view that rosacea is probably a condition which may be due to one or more etiological factors. Each case must therefore be assessed individually with a view to ascertaining which of the many possible factors mentioned above may be of importance. Often a careful history will provide evidence on which a rational course of treatment can be based.

Thus, it is pertinent at the outset to concentrate on the diet and a history of dyspepsia. Particularly, it is often advisable to reduce the intake of tea and coffee and to prohibit alcohol. Most of the patients take too much starchy food and too little fruit. Often they like pickles, chutneys, curries and condiments, which are best avoided. If it is suspected that the patient may have some gastritis and a delayed emptying time of the stomach, acid mixture of gentian B.P.C., ½ fluid ounce (15 ml.) thrice daily after meals, is worth trying. In some cases it is worth while having an x-ray examination and a fractional test meal, although it must be admitted that even in the most suspicious cases the results of these investigations are often disappointingly normal. Many would advise that if there is any suspicion of gastric incompetence riboflavine tablets (3 mg.) should be given thrice daily: I have not been very impressed with this treatment, although it was often given in cases with ocular complications. My belief is that gall-bladder affections and infections are often missed in these patients and in many cases

more attention should be paid to the gall-bladder and to the functions of the liver. Constipation must not be forgotten.

In deference to the theories concerning wind and weather, the patient should be warned that exposure to cold, heat and bright sunlight are bad; some have found that chloroquine, which gives protection against the damaging light rays, is beneficial. Usually it is well tolerated and may be given for several months (particularly in the summer) in the form of 'nivaquine' (chloroquine sulphate), two tablets daily.

In many cases emotional factors are responsible, and I have submitted many to psychiatric investigation and therapy with some measure of success. I think that it is fair to say that the proportion of successes depends upon whether the psychiatrist has a special interest in skin cases or whether he has a comprehensive interest in all fields of medicine. In susceptible persons I am convinced that stresses and anxieties are often of etiological importance, and as many of these are due to life-situations from which there is no escape one is often thrown back on to the use of tranquillizers or barbiturates. By and large, phenobarbitone, in doses of $\frac{1}{4}$ grain (16 mg.) three or four times a day, is as useful as any for this purpose, and should be tried first.

Despite the current scepticism concerning gynæcological factors, if there is any obvious abnormality the patient will be helped if it is successfully treated, and the rosacea may be relieved; certainly in menopausal women suffering from hot flushes the rosacea is relieved if the flushes are controlled.

Desaux (1948) drew attention to the possibility that saprophytic micro-organisms living in the body but not causing symptoms in their habitat might be responsible for a bacterial allergy which could be manifest as rosacea. Aron-Brunetière and his colleagues (1951, 1952) thought that if this hypothesis were correct the responsible organisms would probably be those of the intestinal flora, many of which are affected by chloramphenicol.

Two hundred patients with rosacea complicated by folliculitis of the face and trunk were therefore treated with the drug: the dosage was 1 g. daily for two days, 0.75 g. daily for four days, and 0.5 g. daily for the last two days. In 43 cases partial cure was made complete by a further one or two day courses in which 0.75 g. was given each day. The papulation and pustulation usually faded during the major course of treatment and post-prandial congestion was relieved, but the erythema merely became less intense. Cure or considerable improvement was noted in 48.4 per cent., improvement in 19 per cent. Relapses occurred. Chlortetracycline and oxytetracycline have been similarly used. The authors claim that in one case of ocular and cutaneous rosacea the lesions disappeared during chloramphenicol treatment.

Treatment with chloramphenicol should be remembered but, as the drug can cause blood dyscrasias, the treatment should not be lightly undertaken. Corticosteroids have also been recommended: so far as cutaneous cases are concerned their effects are variable and their use may be dangerous.

LOCAL TREATMENT

In women a good cosmetic mask is not to be despised: it helps morale and seldom irritates the skin of the face. Many like to use calamine lotion with

ichthammol (3 to 5 per cent.) at night, but most prefer Kummerfeld's lotion:—

Precipitated sulphur . . 60 grains (4 g.)
Camphor . . . . . 5 grains (0.3 g.)
Tragacanth . . . . . 5 grains (0.3 g.)
Glycerin . . . . . 10 minims (0.6 ml.)
Lime water . . . . . 240 minims (16 ml.)
Water . . . . . to 1 fluid ounce (28.5 ml.)
To be dabbed on to the face at night.

It is not known whether these lotions have a real effect on the cutaneous capillaries or whether—if the *D. folliculorum* theory is correct—they control the activities of this parasite.

Søbye (1951) has vigorously recommended the following regime:—

For a fortnight—especially in cases in which pustules and papules are troublesome—the face is cleansed only with oil. After cleansing the oil is wiped off, and then some talc powder is dabbed on to the face and then removed so that no oil remains. Then a flesh-coloured shake lotion (e.g. tinted zinc lotion) is dabbed on. This is all done several times daily. After a fortnight massage is started, this being done by a masseuse daily or, if the face is tender, on alternate days. The patient's head is well supported: oil is used as a lubricant: the masseuse uses the volar surfaces of her 2nd, 3rd and 4th fingers employing both hands at once on symmetrical areas, and using light pressure at first but being less lenient later. The fingers make rotary movements over small areas, the pressure of the fingers alternately increasing and lessening, the purpose being to rock the integument to the greatest possible extent in all directions. Fifteen to thirty seconds' treatment suffices for each area. The central areas (e.g. centre of forehead or the nose) are dealt with first at each session and the intermediate and then the outlying areas are massaged. The total time per treatment is about ten minutes. The skin becomes fiery red at once, but the oil is removed, the zinc lotion applied and the redness disappears within an hour. The patients are taught to treat themselves, as the therapy has to continue for several months.

The purpose of the massage is to remove œdema and infiltrations and to break down fibrosis. Søbye claims that of 50 cases, 22 were cured, 20 considerably improved, whilst eight were 'not much better'.

Cryotherapy was discussed by Lipman Cohen (1948). He stated that it caused vasodilatation followed by vasoconstriction, with the obliteration of some of the superficial vessels.

Whilst a cryocautery or a ball of snow may be used, Cohen advocates that a towel should be put round the patient's neck (lest some of the snow fall down the neck) and a slush prepared by dropping a few drops of acetone on to carbon-dioxide snow until the latter looks like colourless water ice. A wooden spatula round which three turns of cotton bandage have been wound must be ready; this is dipped quickly into the slush which is brushed over the affected areas with very slight pressure twice so that the slush is in contact with the skin for one second. If dealing with dark, seborrhœic, young skin the application may be slightly heavier than on thin or elderly integument. On the thicker areas the skin should be momentarily blanched. The skin becomes red, unsightly and slightly painful for a few hours. By the following day, except for mild peeling, all signs of reaction should have disappeared but there may be some blistering if the operator has overestimated the resistance of the skin.

Treatment is usually given once a fortnight for four to eight weeks and nearly always leads to much improvement but complete cure is not

guaranteed. Lipman Cohen does not regard cryotherapy as a sole treatment: other measures must proceed at the same time.

Finally, it should be mentioned that x-ray therapy (both for cutaneous and ocular rosacea) has its advocates, that rosaceous keratitis is usually treated with cortisone or hydrocortisone eye-drops, and that rhinophyma is best dealt with by plastic surgery.

I have to thank Drs. Peter Borrie and E. Lipman Cohen for their suggestions, and the photographic department of St. Bartholomew's Hospital for the illustrations.

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THE DIAGNOSIS AND TREATMENT OF TINEA PEDIS

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It is not within the compass of this article to discuss the rarer deep fungus infections such as blastomycosis, sporotrichosis, and Madura foot, but to confine the scope to diseases caused by fungi of the dermatophyte group which invade only the superficial skin and by the yeast-like fungus *Candida albicans*.

The existence of fungus infections of the feet is well known to most lay people, as is shown by the many terms such as 'athlete's foot', 'surfer's toe', and 'Hong Kong rot', and of course dermatologists have not been behindhand in nomenclature, with names such as tinea pedis, dermatophytosis and epidermophytosis. Strictly speaking, the last name should be applied only to those cases from which an epidermophyton fungus has been isolated by culture, for by no clinical means can this type be differentiated from other infections such as those due to trichophyton, *Candida albicans* and even occasionally microsporon.

Cultural examinations of 200 cases of foot dermatophytosis were made by Hall (1956) with the following findings:—

Trichophyton mentagrophytes	50.4 per cent.
Trichophyton rubrum	38.1 per cent.
Epidermophyton floccosum	6.5 per cent.
Candida albicans	5.0 per cent.

He observed that males were more often affected than females, in a proportion of 143 to 57 cases, and that in 12 patients *C. albicans* and *E. floccosum* were found with either *T. rubrum* or *T. mentagrophytes*.

CLASSIFICATION

In the absence of cultural proof, it is not possible to determine by clinical or microscopic study the type of fungus present, and it is worth noting that infections with *T. rubrum* are notoriously resistant to therapy. For the practical purpose of differential diagnosis, however, fungus infections of the feet may be placed in four main clinical groups, although more than one of these may be present in the same case.

Macerated lesions, usually found as sodden, white, malodorous epidermis in the webs of the toes. Any of the fungi mentioned can produce this appearance, but it is more often found in *C. albicans* and *T. mentagrophytes* infections (fig. 1).

Vesico-pustulo-squamous lesions, often arranged in a circinate pattern on the insteps or sides of the foot, or spreading from the toes on to the dorsum.

Squamous lesions, occurring as desquamation of the interdigital areas and

from there spreading over other areas of the foot, especially the soles (fig. 2).

Keratotic lesions, associated with hyperkeratosis and fissuring, chiefly on the sole.

In all these types, the toenails may be involved to a greater or lesser degree, but the consideration of ringworm of the nails is outwith the subject of this article.

Even though fungus can be demonstrated either microscopically or culturally, this does not necessarily imply that all or even the greater part of the patient's dermatosis is due to the ringworm, as is shown by the following case:—

A young man was seen with a vesico-bullous eruption involving the toes, heels and sides of the feet. Many mycelial threads were found on microscopic examination of the roofs of vesicles, but the youth gave a family history of the asthma-eczema syndrome and had a tendency to hay fever. The rash had appeared shortly after he had worn a new pair of rubber shoes, and later patch-tests to this rubber provoked a strong positive reaction. In fact, this patient had not only an active fungus infection, but also a contact dermatitis and a cutaneous expression of his inherited allergic tendency.

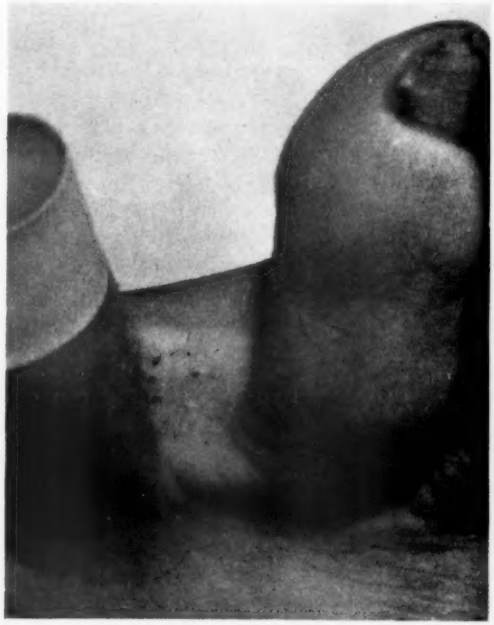

FIG. 1.—Tinea interdigitalis.—Macerated skin in web of fourth and fifth toes, in a patient with hyperkeratosis of palms.

DIFFERENTIAL DIAGNOSIS

Macerated lesions.—The presence of sodden interdigital skin is often presumed to be invariably due to a fungus infection, but this is by no means true. Quite often *hyperidrosis* of the feet (sometimes called symmetrical lividity of the soles) is mistaken for a fungus infection and treated accordingly with poor results. In these cases, usually young men, there is often a history of prolonged standing on a hard floor, perhaps under warm conditions, and the wearing of shoes with thick rubber soles. The skin of the weight-bearing part of the soles and toes is cyanotic, and may show pitted macerated areas; in the webs white hypertrophic epidermis is found and it is this which is often mistaken for tinea. *Intertrigo* or *flexural infective*

eczema may occur between the toes (fig. 3), just as it can appear in other areas such as the natal cleft or submammary regions. Similar lesions may be found in other flexures and no mycelia or spores would be found on microscopic examination of scrapings. Maceration of the interdigital areas can be found in association with soft *corns* and *warts*, so that ringworm infection is wrongly diagnosed.

FIG. 2.—Squamous tinea of the sole.

Vesico-pustulo-squamous lesions.—Two distinguished American authors (Becker and Obermayer, 1940) remark that:—

'the relative increase [of such eruptions] has arrested the attention of the medical profession to such an extent that it has become "ringworm-conscious"; the formerly universal diagnosis of dyshidrosis has given way to the equally universal diagnosis of ringworm of the feet whenever a vesicular eruption of this region is present . . . Not more than about 50 per cent. of vesicular lesions of the feet in adults can be proved to be due to fungi. In children, the percentage is even smaller . . . '.

Eczematous reactions are often mistaken for dermatophytosis, especially *contact dermatitis*, which is often caused by footwear (e.g. rubber, dyes, glues). In these cases, the rash usually first appears on the dorsum of the great toes, then on the other toes, extending along the sides of the feet and over the heels (fig. 4). The dye of socks and stockings may be the offender, but also produce a typical dermatitis on other parts of the limbs. Not so common are the cases caused by nickel- or chrome-plated arch-supports and by rubber pads or insoles, and the eruptions due to 'iodine-medicated socks' have not been seen in recent years. *Pompholyx* or dyshidrosis may be difficult to distinguish from ringworm; the history of the case may be of help: e.g. a familial tendency to hay fever or asthma; recurrent attacks either at certain seasons such as spring and autumn or after a period of mental stress. In contradistinction to fungal infections, the eruption is symmetrical and mainly vesicular or bullous in character. *Post-traumatic infective eczema* (infectious eczematoid dermatitis) is sometimes located on the feet, and may appear as an impetiginous eruption, perhaps originating on areas rubbed by ill-fitting shoes, or as circinate patches with an irregular spreading edge. An example of this type is *dermatitis repens*, due to a staphylococcal infection, spreading slowly beneath the stratum corneum, and producing an undermined edge not unlike a ringworm, and tense pustules surrounded by a zone of inflammatory reaction (fig. 5). Other causes of vesicular or bullous eruptions of the feet include *scabies*, of which

other evidence should be sought on the patient and his close associates, and *epidermolysis bullosa*, in which bullæ arise following trauma of the dorsa or soles.

The group of recalcitrant pustulo-squamous dermatoses which may closely simulate dermatophytosis include *pustular bacteride*, *pustular psoriasis*, and *acrodermatitis perstans pustulosa*. No mycelium can be discovered on repeated microscopic examination of scales, and, as the pustules are sterile, no growth of fungus or bacteria is obtained on culture. Pustular bacteride appears gradually on the plantar aspect as one or more patches, erythematous, circumscribed, with laminated scaling and discrete deep pustules which dry up and turn brown as they come towards the surface (fig. 6). Pustular psoriasis shows a similar picture, but evidence of psoriasis may be discovered on other parts of the body such as the nails, the scalp or the elbows. With acrodermatitis perstans pustulosa, the pustules are more superficial, even subcorneal, there is more tendency to exudation and the toes are more often affected. *Keratodermia blenorrhagica* and *Reiter's disease* are other resistant conditions which can provoke sterile pustulation, but hyperkeratosis is more pronounced and other symptoms and signs are almost invariably present (fig. 7).

FIG. 3.—Flexural infective eczema, showing interdigital maceration in a patient with exfoliative seborrhœic dermatitis.

FIG. 4.—Contact dermatitis, with a distribution characteristically due to dye in shoes.

Squamous keratotic lesions.—These are best considered together, as the diseases which resemble them show varying degrees of hyperkeratosis. Although *psoriasis* tends to occur on characteristic sites, it can at times be localized to the soles alone, though typical nail changes may be detected (fig. 8). The patches may be more hyperkeratotic than those found on other areas and it may be possible to produce 'candle grease' scaling on scraping them. Sometimes the only method to establish the diagnosis is to take a biopsy for histological examination. Such biopsy material taken to confirm

or exclude a fungus infection can be stained with the periodic acid-Schiff reagent (Hotchkiss-McManus stain): this is most useful in demonstrating fungi (Kligman and Mescon, 1950).

Lichen planus may affect the feet, either as lilac annular patches composed of shining polygonal scaly papules, or, on the sole, as violaceous scaly hypertrophy, sometimes with alteration of the nail plates. Manifestations of this condition should be searched for on other parts of the skin and on mucous membranes. *Lichen simplex chronicus* (*circumscribed neurodermatitis*), with a history of bouts of intense pruritus, rarely occurs on the soles, but can occur on the dorsum of the feet and toes (fig. 9). The patches are lichenified, with a somewhat ill-defined margin and with accentuation of Wickham's striæ and often with excoriations. Another chronic dermatosis is *keratodermia climactericum*, found in postmenopausal women, and occurring on the soles as circinate hyperkeratotic plaques with deep and painful fissuring. In middle-aged or elderly men, a chronic *keratotic eczema* may involve the soles and may be extremely difficult to differentiate from a keratotic tinea. In these days, *syphilides* are seldom seen, but the possibility must always be considered. Whilst papular syphilides never occur only on the feet, the squamous syphilide can closely imitate a mycotic infection, as it is circinate with a well-defined margin. *Drug eruptions*, especially those due to the heavy metals and mepacrine, may start on the soles, as desquamation or keratosis, and the history of their ingestion will aid in the diagnosis.

FIG. 5.—Dermatitis repens, showing undermined spreading edge and healing pustules, from which *S. aureus* was cultured.

FIG. 6.—Pustular bacteride, with desquamation and discrete sterile pustules.

Accurate diagnosis of tinea pedis must be based on sound evidence, as there are so many pitfalls. The *history* may give a valuable lead: e.g. of a stay in a hot climate; of a communal life in a school or the Services or as a

member of an athletic club; or of previous attacks proved to be due to a fungus. As well as relying on the *clinical appearance* of the rash on the feet, the physician should examine other areas of the body such as the groins and axillæ for evidence of tinea or other disease. In every case an attempt should be made to demonstrate mycelium *microscopically*, either in a potassium hydroxide or a stained preparation.

FIG. 7.—Reiter's disease, with erythematous hyperkeratotic patches on sole and interdigital involvement.

The former, in a 15 to 30 per cent. solution, is placed on a slide on which scales or cuttings from the vesicle roofs have been set. The slide is heated sufficiently to dissolve the keratin and then examined under a medium-power lens with the condenser retracted (fig. 10). Stained specimens have little advantage over these except that they can be kept for future reference. Of the many suitable stains, the Hotchkiss-McManus one referred to previously is particularly useful for staining biopsy material. *Histological sections* otherwise show no typical features, either an eczema reaction or a non-specific inflammatory one being found. *Cultures* on suitable media may reveal the presence of fungi not detected by other means and should be resorted to in doubtful cases (fig. 11). When pustulation occurs, *bacteriological examination* may show no growth of organisms or the presence of pyogenic ones, secondary invaders of a tinea or the cause of an infective eczema.

FIG. 8.—Psoriasis affecting the heel.

TREATMENT

In treating tinea pedis the most important fact to realize is that therapy must not be merely an attempt to destroy by means of more and more potent fungicides the ringworm invading the superficial layers of the skin. More often than not potent chemicals applied to the skin do far more harm than good. The deciding factor in the development of an active fungus infection is the cutaneous resistance, which can be diminished in many ways. *Candida albicans* flourishes in a moist sweet medium so that diabetics are particularly prone to develop such yeast infection. Tinea is mainly a disease of cleanly people, as those who seldom wash their feet not only do not expose themselves to infection, but also do not alter the pH of the skin by using soap and water frequently.

'Obviously the primary infection of the skin must be exogenous but thereafter endogenous sources predominate as the cause of exacerbations' (Strauss and Kligman, 1957).

A man may have been an active carrier of fungi on his feet for years before he develops clinically active disease.

FIG. 9.—Lichen simplex chronicus, with lichenification and excoriations.

No practitioner should promise a patient that he will cure tinea pedis although he may be able to remove the symptoms and signs to the satisfaction of his patient. Even though all infected socks and shoes are destroyed the fungus still remains dormant in skin or nails. Disinfection of footwear is therefore of little avail and may even provoke a chemical reaction on the already irritable skin.

PROPHYLAXIS

From my experience with Service units in Britain and in warmer countries, I believe that much can be done to prevent spread of infection within a community. The provision of foot baths containing 1 per cent. sodium hypochlorite solution in showers or bathing places, where each person must immerse his feet before and after bathing, probably has little effect on the actual tinea pedis, but kills the fungi in the scales which are broadcast from infected persons. The provision of a simple foot powder used by each individual night and morning can prevent spread of the disease. Fungicidal powders such as dusting powder of zinc undecenoate B.P.C. are no more effective than mildly acid ones such as compound dusting powder of salicylic acid B.P.C., which contains 3 per cent. salicylic and 5 per cent. boric acid. Clogs such as are worn in the locker rooms of American country clubs have not been proved to be of real value.

LOCAL THERAPY

The discovery of nystatin during the search for new antibiotics marks a real advance in therapy, as this substance has a remarkable lethal effect on yeast-like organisms such as *Candida albicans*, and can be given orally as well as applied locally. When a skin disorder is caused by *Candida albicans* the application of nystatin ointment is extremely effective and in cases involving large areas of skin and other organs the drug in a dose of four tablets (each tablet contains 500,000 units) a day often gives excellent results. Other antibiotics have shown strong fungicidal activity *in vitro*, but so far there has been no report of highly successful results in cases of tinea pedis

due to trichophyton or epidermophyton infection. In the United States, other antibiotics—trichomycin, amphotericin B and eulicin—have been considered the most promising for clinical use (Blank, 1957), but six patients with resistant tinea interdigitalis treated by me four years ago with tricho-

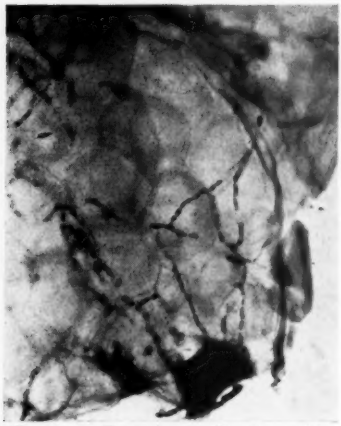

FIG. 10.—Fungal mycelia, from skin scrapings, stained lactophenol blue. Culture might show either microsporon, trichophyton or epidermophyton. (× 330)

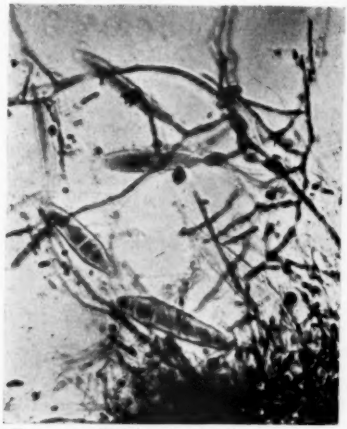

FIG. 11.—Trichophyton, from culture on Sabouraud's glucose agar, showing multiseptate clavate thin-walled macrogonidia. (× 320)

mycin ointment showed no improvement and, in 1957, 1 per cent. griseofulvin ointment supplied by Imperial Chemical Industries proved to be no better than orthodox preparations in a controlled series of cases in a boys' boarding school (Peterkin and Brewster, 1957). Yet it seems possible that in the future fungus infections of the skin may be eradicated by some antibiotic given parenterally.

For macerated interdigital tinea, powders, paints or wet dressings are preferable to ointments. Thorough dusting of the webs and soles with a mildly acid powder, such as salicylic acid compound or zinc undecenoate powder, may be adequate to control the less advanced infections, but in the more chronic ones weak or strong iodine solution depending on the case, 2 per cent. silver nitrate in nitrous spirits of ether, and Castellani's paint are appropriate treatment. This fuchsin paint should not be prescribed as paint of magenta B.P.C., but made freshly according to the original prescription:—

Saturated alcoholic solution of basic fuchsin	10.0
Phenol (5 per cent. aqueous solution)	100.0
Filter and add boric acid	1.0
After 2 hours add acetone	5.0
After 2 more hours add resorcin	10.0

Keep in a dark well-stoppered bottle.

When vesiculation or pustulation is apparent or if the infection is in an acute phase, treatment should be precisely the same as for a case of acute infective eczema, and the more potent fungicides avoided. Vesico-bullous eruptions generally respond well to bed rest and bags made of calico and filled with one of the powders mentioned, but most cases are best treated with wet dressings of 5 per cent. strong solution of lead subacetate or aluminium acetate lotion used undiluted. Except in hot countries these compresses are best covered by impermeable material such as polythene or oil-silk, and changed at least twice daily. Silver nitrate (0.5 per cent.), though apt to stain clothes, is particularly useful in the presence of a septic infection.

Once the acute stage has subsided and the vesicles or pustules have dried up, one of the higher fatty acid fungicides can be prescribed; e.g. ointment of zinc undecenoate B.P.C. or 'sopronol' ointment, although Lassar's paste is often quite as effective. In the infected eczematized type of tinea, quinoline derivatives are especially useful, e.g. 'quinolor' compound ointment, 'vioform' ointment, 'steroxin' ointment, but it is advisable to add 1 per cent. hydrocortisone to them, not only to control pruritus and inflammation, but also to prevent the reaction sometimes caused by these useful drugs.

When pyogenic infection is associated with the dermatophytosis, the use of antibiotics such as penicillin, chlortetracycline and oxytetracycline, whether applied locally or used internally, is strongly contraindicated, for they are apt to provoke widespread reactions in the form of dermatophytides. In their stead, sulphonamides such as 'sulphatriad' can be administered orally.

For the squamous or keratotic types of ringworm, greasy preparations are acceptable, and the famed Whitfield's ointment is still second to none. Compound benzoic acid ointment B.P.C. is not so effective as the original prescription, as its base is emulsifying ointment instead of:—

Salicylic acid	3.0
Benzoic acid	5.0
Coconut oil	50.0
Soft paraffin	50.0

For the most resistant intractable fungus infections, which are often caused by *T. rubrum*, persistent treatment with powerful fungicides is required. Of these, 'asterol' ointment and dithranol, ranging in strength from 0.5 per cent. in Lassar's paste to 2 per cent. in soft paraffin, are among the most effective.

CONCLUSIONS

Accurate diagnosis is a prime essential in dermatoses of the feet, as many can closely simulate tinea pedis, and inappropriate treatment leads to a chronic disabling eczema.

Even with a proved fungus infection, it is often advisable to treat it as an ordinary infective eczema in the initial stages, and to use fungicides once the skin is healing well. The main objective is to aid healing power in every possible way.

The effectiveness of nystatin in yeast infections may indicate that some new antibiotic may become a powerful weapon in the treatment of ringworm, not only by local application but also parenterally. So far some antibiotics show marked fungistatic action *in vitro* but have been of little value clinically. Penicillin, chlortetracycline and oxytetracycline should not be used to treat secondary pyogenic infection, because of their tendency to cause acute exacerbation of the fungus infection.

Despite the introduction of many new fungicides, Castellani's paint and Whitfield's ointment have not been superseded. The former can be used in the presence of maceration and vesiculation and the latter in the scaly or hyperkeratotic types. Higher fatty acid ointments and powders containing undecylenic or propionic acid are often effective and seldom cause chemical reactions, an advantage which is not shared by some of the newer products.

Acknowledgement is due to Dr. M. Tatz for fig. 10 and 11; to Mr. T. C. Dodds, F.R.P.S., department of medical photography, University of Edinburgh, for fig. 2, 3, 5, 7, 8 and 9; and to Mr. D. A. Franklin, Bangour Hospital, for fig. 1, 4 and 6.

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TUBERCULOSIS OF THE SKIN

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CUTANEOUS tuberculosis is much rarer today than it was in the first quarter of this century. The decrease began after the 1914-18 War and the credit for it must be given mostly to improved standards of milk production, to better housing conditions, and to earlier diagnosis and better control of both pulmonary and non-pulmonary tuberculosis.

Infection of the skin with tubercle bacilli may cause various reactions according to the source and route of infection and the age and immunological state of the patient at the time. There may be an exogenous primary infection, an exogenous or endogenous super-infection, or a reaction of sensitivity—a tuberculide.

PRIMARY TUBERCULOSIS OF THE SKIN

When a primary infection takes place in the skin with tubercle bacilli, a tuberculous chancre results, the regional lymph node enlarges and softens and the Mantoux reaction changes from negative to positive. Primary lesions occur mostly in children but may become relatively commoner in adults in view of the increasing proportion of negative Mantoux reactors among them. Primary tuberculosis sometimes occurs within the mouth or within the conjunctival sac. Thus, Miller (1953) described 28 examples of external primary lesions, of which 20 were cutaneous, 5 ocular, and 3 oral.

In the skin the primary lesion is often banal: a group of papules or a painless crusted patch resembling impetigo, at the site of an abrasion, wound or coccal infection. The lesion may ulcerate but does not suppurate and it does not heal after the local application of antibiotics. 'Apple-jelly' nodules may develop, particularly at the margin. The regional lymph node enlarges and softens (fig. 1). Lymphadenitis may be the presenting symptom if the parent regards the primary lesion in the skin as too trivial to need attention.

A primary lesion persists for several months and lupus vulgaris may originate from it or erythema nodosum follow it. Miliary tuberculosis is a very rare sequel. The chancre usually forms at a site exposed to trauma: on the face, a hand, knee or foot, with pre-auricular, cervical, axillary or inguinal lymphadenitis. The lymph node gradually softens and, unless the fluid is aspirated from it, the overlying skin may break down, with the discharge of a blood-stained, sero-purulent fluid. Scrofuloderma may follow. Tubercle bacilli may be recovered from the fluid or be seen on skin biopsy in a tuberculoid granuloma.

A primary lesion in the conjunctiva causes persistent œdema of the lids, conjunctivitis with a granular thickening of the conjunctiva and a painless

pre-auricular adenitis. Within the mouth, a primary infection produces relatively painless ulceration of the gum, cheek, tongue or lip, with submandibular lymphadenitis. The trauma of a tooth extraction or an alveolar abscess may provide the portal of entry. Primary infection may also occur on a tonsil.

Treatment.—There may be a known tuberculous contact. If not, search should be made for a human or bovine source of infection. The child should be well fed. Some recommend that active treatment should be withheld, so as to allow the patient to develop a natural immunity, with healing of the primary lesion. Unfortunately, the natural course is prolonged and there is always a risk that the infection may spread beyond the first chain of lymph nodes. For these reasons it may be wiser to treat with isoniazid and streptomycin or PAS once lymphadenitis has developed. Chemotherapy combined with excision of the regional lymph node while it is still firm has been performed in some cases reported by Miller and Cashman (1955), with considerable reduction in the duration of morbidity.

FIG. 1.—Primary tuberculosis of the skin. A tuberculous chancre on the eyebrow, with pre-auricular adenitis.

REACTIONS FOLLOWING VACCINATION WITH BCG

BCG vaccination is designed to produce a primary tuberculous chancre of attenuated virulence, followed by a self-limiting infection and Mantoux conversion. The usual BCG reaction, according to Ustvedt (1956), is a 'grossly visible primary focus in the skin and a less easily ascertainable regional adenitis'.

Marcussen (1954) reported the development of lupus vulgaris around the site of vaccination (fig. 2) in six patients seen by himself and others. This complication is very rare, considering the large number of vaccinations that are done.

Hartston (1958), from experience of 65,000 BCG vaccinations of 13-year-old London children, estimates the incidence of lupus nodules measuring between 2 mm. and 6 mm. and developing between six and twelve months after vaccination as 1 in 3000 vaccinations. All these lesions healed spontaneously within six months. Gordon (1957) observed lymphadenitis proceeding to caseation and abscess formation after 1.4 per cent. of vaccinations of contacts. Erythema nodosum occurred five times and phlyctenular conjunctivitis three times after 32,000 vaccinations.

Jørgensen and Horwitz (1956) have analysed the complications of BCG vaccination as seen in patients referred to the Finsen Institute. In 100 such patients there were 87 with regional adenitis, suppuration occurring in 71 of them and scrofuloderma in three. Tuberculides had developed in 14 patients and 10 suffered from lupus vulgaris, 10 from lupoid affection (reminiscent of lupus vulgaris but without typical nodulation or unquestionable progression), and 10 from Koch's phenomenon (immediate acute reaction, with ulceration). In these last three groups all the patients were over 15 years of age. Other complications included lymphangitis and subcutaneous abscess formation, and the commonest non-specific complications were localized eczema and keloids.

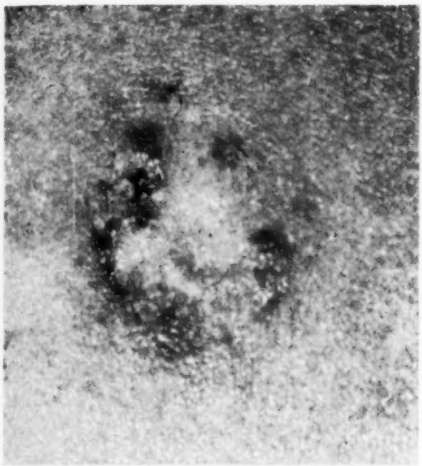


FIG. 2.—Nodules of lupus vulgaris around a BCG vaccination scar.

Tuberculous complications after BCG vaccination run a milder course than spontaneously developed skin tuberculosis, and therefore active treatment is seldom required. Complications are commoner and severer among the revaccinated than among persons vaccinated for the first time (Jørgensen and Horwitz, 1956).

TUBERCULOSIS VERRUCOSA CUTIS

Warty tuberculosis develops when tubercle bacilli get in through a break in the skin of an adult whose tissues have previously reacted to tuberculous infection. The infection arises from contact with an infected person, tuberculous tissue, an infected human or animal cadaver or infected fomites such as handkerchiefs. It may also occur from autocontamination of the skin by infected discharges from the respiratory, gastro-intestinal or genito-urinary tracts. The lesion is usually on an exposed part, particularly the hand (fig. 3), but it may also occur on the buttocks (fig. 4).

Warty tuberculosis is dusky coloured and suggests a slightly infected wart. It may spread in annular fashion, with central scarring. Tubercle bacilli may be recovered from the discharge, an important point in the differential diagnosis from sporotrichosis or blastomycosis. The histological appearance is usually non-specific, with papillomatosis overlying a dermis which is heavily infiltrated with polymorphonuclear cells and lymphocytes but with giant-cell systems few or absent. A mild regional lymphadenitis is often present. Occasionally a chain of subcutaneous swellings develops along the course of lymphatics. These swellings soften and the overlying skin breaks down, resulting in a clinical picture resembling sporotrichosis (fig. 5).

Treatment.—Warty tuberculosis from an extraneous source responds well to isoniazid in a dose of 300 mg. daily, which should be continued for at

least a year. Search should be made for a visceral focus of tuberculosis, even when the evidence suggests an external source of infection. When warty tuberculosis is autogenous, treatment is directed also to the visceral infection and consists of some combination of isoniazid and streptomycin or PAS.

TUBERCULOSIS CUTIS ORIFICIALIS

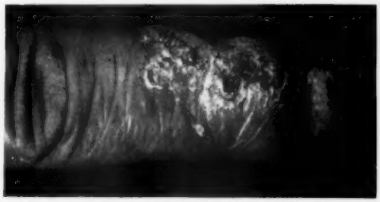


FIG. 3.—Warty tuberculosis of the finger.

Tuberculous ulceration may occur within the mouth by contamination from tuberculosis of the lungs or larynx, at or near the anus from tuberculosis of the bowel, or on the external genitalia from genito-urinary tuberculosis. The ulcers are usually about 5 mm. in diameter and may be painful or painless, depending upon whether they are exposed to movement or trauma, or whether they become secondarily infected. They have shelving edges and are circular or irregular in shape, with grey, non-granulating bases (fig. 6). Spontaneous healing does not occur and there may be some regional lymphadenopathy. The diagnosis is obvious when visceral tuberculosis is known to exist but otherwise it may not be considered. Tubercle bacilli may be recovered by scraping the base of the ulcer or they may be apparent in a biopsy specimen which shows a tuberculoid granuloma.

Treatment.—Treatment is that of the visceral tuberculosis. If healing is delayed the ulcer may be excised or, if it is too large, treated by diathermy destruction.

FIG. 4.—Warty tuberculosis of the buttocks in a patient with pulmonary tuberculosis.

SWIMMING-BATH GRANULOMAS

In 1948, MacCallum and his colleagues described chronic ulcerative skin lesions with overhanging edges and marked peripheral and basal induration, due to an acid-fast organism which was not *Mycobacterium tuberculosis* and which they named *Mycobacterium ulcerans.*

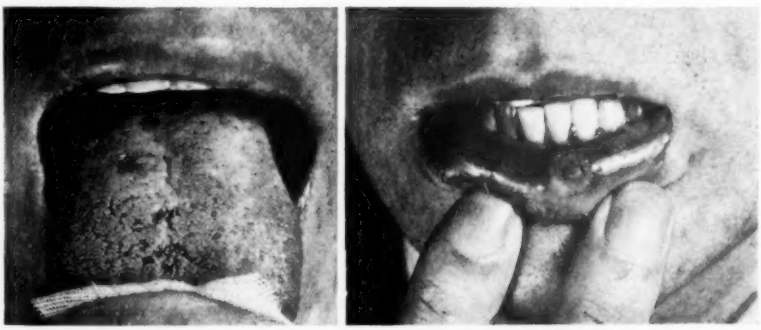
Hellerström (1951) and Cleveland (1951) described cutaneous granulomas acquired from abrasions received in swimming-baths. In a case reported by Brück

(1952) tubercle bacilli of human type were recovered. In another case a swimming-pool attendant was found to be suffering from open pulmonary tuberculosis. In other cases with crusted non-specific sores on the nose or elbows, acid-fast bacilli of attenuated virulence have been recovered. It has been suggested that these might be *Mycobacterium tuberculosis*, modified by chlorination and the cooler temperature,

FIG. 5.—Warty tuberculosis of the back of the hand, with subcutaneous tuberculous abscesses and scars thereof on the forearm and arm. The patient had pulmonary tuberculosis. (Patient of Dr. J. S. Pegum).

or that they might be *Mycobacterium smegmatis*, *Mycobacterium marinum* or *Mycobacterium ulcerans*.

Linnell and Norden (1951, 1952, 1954) investigated an epidemic of swimming-pool lesions of the skin in a Swedish town, and recovered an acid-fast organism



(a) (b)

FIG. 6.—*Tuberculosis cutis orificialis*. Tuberculous ulceration of the dorsum of the tongue (a) and of the lower lip (b) in a patient with pulmonary tuberculosis.

which resembled *Mycobacterium ulcerans*, in that it grew best at 31°C. but differed from it in other respects. The organism, which they named *Mycobacterium balnei*, was not pathogenic to guinea-pigs and was inhibited *in vitro* by streptomycin but not by isoniazid. The lesions took up to two years to heal and two patients were observed to become tuberculin positive at the time of appearance of the lesions. Weed, Keith and Needham (1956) have described eight cases of caseating cervical adenitis in children, due to non-tuberculous 'saprophytic' acid-fast bacilli.

It seems clear therefore that acid-fast bacilli other than those of leprosy and tuberculosis can cause tuberculoid disease in man. Culture and guinea-pig inoculation are necessary for identification of the acid-fast bacilli recovered. In some cases of swimming-bath granuloma no acid-fast bacilli have been recovered. It has been thought that the lesions in these cases were silicate granulomas.

FIG. 7.—Lupus vulgaris of the ear lobe and adjoining skin, showing the appearance on diascopy.

FIG. 8.—A group of nodules of lupus vulgaris on the cheek.

TUBERCULOSIS LUPOSA (LUPUS VULGARIS)

New cases of lupus vulgaris in children are rare nowadays, but many middle-aged and elderly patients remain who show evidence of its past damage, and resulting disfigurement. Patients with lupus vulgaris do not often have active pulmonary tuberculosis. Griffith (1922) suggested that virulent strains of bacilli become attenuated as a result of their residence in the skin, perhaps because of their exposure to light in this situation. Lupus vulgaris may follow the entry of tubercle bacilli from without but it more often arises by direct spread or by lymphatic spread from a focus within the nose, or by outward spread from a deeper focus in bone, joint or lymph node. Hæmatogenous lupus is a rare phenomenon, usually in a debilitated child after an attack of measles. The development of lupus presupposes a previous primary focus of infection, in lung or skin.

The earliest lesion is a solitary, translucent, 'apple-jelly' nodule. Examination through a piece of glass pressed to the skin so as to obliterate the

cutaneous vessels makes the 'apple-jelly' appearance more obvious (fig. 7) and helps in the differential diagnosis from the juvenile melanoma, a benign lesion which may appear on the face and enlarge during childhood. The overlying epidermis is usually atrophic in lupus and as the lesion enlarges a

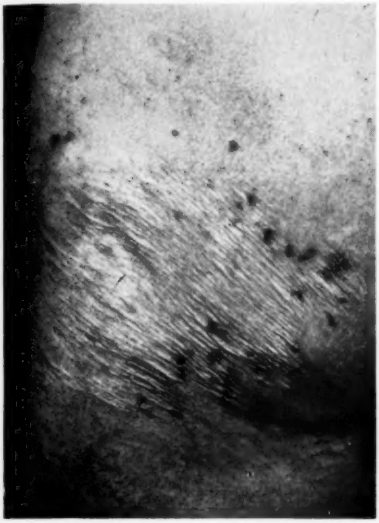


FIG. 9.—Multiple nodules of lupus vulgaris recurring in a treated atrophic scarred patch.

FIG. 10.—Secondarily infected lupus vulgaris with destruction of the ala nasi and perforation of the nasal septum. The condition responded well to isoniazid and the local application of an antibiotic.

circular or irregular group of nodules results (fig. 8). Individual nodules are often visible in the margins of extensive areas of scarred, long-existent, treated lupus (fig. 9). A scarred area of past lupus may be irregularly pigmented and depigmented, with telangiectasia, the result, in part, of past treatments, particularly x-rays. The differential diagnosis from lupus erythematosus is sometimes difficult. In general, the latter tends to start more in adult life, to be symmetrical with multiple lesions spreading centrifugally, and with central scarring, much dyskeratosis and an absence of deformity other than cutaneous, whereas lupus vulgaris often destroys cartilage with much deformity (e.g. ectropion, deformity of the pinna, microstomia) (fig. 10). Syphilis, leprosy, leishmaniasis, sarcoidosis, halogen granuloma, lupoid sycosis and cutaneous reticulosis also have to be excluded by means of a careful clinical, histological, radiological and bacteriological assessment.

Treatment.—Good food and housing are important. Specific treatment has been transformed and simplified by the introduction of isoniazid. The

daily dose is 4 mg. per kg. of body weight. For an adult a daily dose of 300 mg. is adequate and it must be continued for at least fifteen months. With this dosage side-effects are exceptional. Clinical clearance is indicated by the disappearance of all apple-jelly nodulation and scaling, a soft, slightly

(a) (b)

FIG. 11.—(a) Healed lupus vulgaris of the nose, leaving destruction of the nasal cartilages. (b) After rhinoplasty, performed by Mr. Charles Heanley, from a donor site on the right side of the forehead.

pigmented scar remaining. Periodic re-inspection of the lesion is necessary for at least five years after completion of the course of treatment before the condition can be regarded as cured. Suspected recurrences have to be differentiated from areas of pigmentary change or of dyskeratosis, particularly in those patients who have previously been treated with x-rays. As an aid to diagnosis an attempt can be made to bore into the suspected nodule with a sharply pointed orange stick, the tip of which has previously been dipped into some acid nitrate of mercury. If the surface of the skin collapses and a small cavity is opened up, the diagnosis of recurrence is confirmed and the acid will at the same time destroy the nodule, perhaps making a further course of isoniazid unnecessary.

Finn and Rogers (1955) have surveyed the literature up to 1954 on the treatment of cutaneous tuberculosis (mostly lupus vulgaris) with isoniazid. I am in complete agreement with their opinion that isoniazid alone is adequate in the treatment of cutaneous tuberculosis uncomplicated by visceral tuberculosis. The tubercle bacilli in lupus vulgaris are usually of attenuated virulence (Griffith, 1919, 1922), and there is no clinical evidence to suggest that resistant strains of tubercle bacilli develop when isoniazid is used alone in the treatment of lupus vulgaris. Furthermore, the patient is

saved from the possible side-effects of other anti-tuberculous drugs. When pulmonary tuberculosis or some other visceral form of tuberculosis coexists with the cutaneous tuberculosis it is necessary to give combined treatment with isoniazid and streptomycin or PAS. Treatment of lupus vulgaris with calciferol or by local or general ultra-violet irradiation is today obsolete and rarely indicated.

Complications.—Lupus vulgaris may be complicated by secondary infection, disfigurement (ectropion, deformities of nose, ear, mouth or limb) or by squamous epithelioma or sarcoma. Secondary infection can be dealt with by antibiotics, but the lymphœdema which may follow recurrent, inadequately treated secondary streptococcal infections is irreversible. Some deformities can be effectively relieved by plastic surgery under a protective cover of isoniazid. The results of rhinoplasty are particularly gratifying (fig. 11). As a prophylactic measure it may be wise to excise and graft areas of dyskeratotic skin before squamous epitheliomatous changes supervene. Squamous carcinoma or sarcoma can be successfully treated in their early stages by surgery and plastic repair or by radiotherapy. When more advanced, they may prove intractable and palliation alone is possible.

In the past, lupus erythematosus has been regarded as a tuberculous manifestation by some authorities. Few hold this view today. Nevertheless, occasionally lupus erythematosus follows undoubted lupus vulgaris on the face. Thorne (1957) described such a case and I have seen a woman with lupus erythematosus on the face and neck, which responded to chloroquine, the skin lesions having developed at the site of old scrofulodermatous lupus vulgaris which had been treated by ultra-violet irradiation some 30 years before. This happening might be chance or a direct sequel to the repeated trauma of intense ultra-violet irradiation.

TUBERCULOSIS COLLIQUATIVA

In scrofuloderma, a painless pale pink or bluish swelling appears in the neck, the skin breaks down and an ulcer is formed with overhanging edges. Sinuses and epidermal bridges may form and tubercle bacilli may be recovered from the blood-stained, sero-purulent discharge. Senile tuberculosis occasionally presents in this way. Tuberculosis colliquativa may also occur along the course of lymphatics or at other than cervical lymph nodes and it may complicate a primary infection, warty tuberculosis or BCG vaccination. The diagnosis has to be made from acne conglobata, gumma, actinomycosis and sporotrichosis.

Scrofuloderma may respond to isoniazid alone but it may be advisable to give combined treatment with isoniazid, streptomycin and PAS.

TUBERCULIDES

Tuberculides are symmetrical eruptions, occurring in individuals who are hypersensitive to tuberculin. They are indicative of an active tuberculous focus elsewhere in the body. In the skin lesions themselves tubercle bacilli are few in number or it may not be possible to find any.

Erythema nodosum is the commonest tuberculide following a primary complex in lung or skin or BCG vaccination, but there are causes for it other than tuberculosis, including streptococcal and meningococcal infections and sarcoidosis. In adolescents and young adults tuberculosis should

FIG. 12.—Tuberculosis indurativa.—Scabbed tuberculous gummas and scars on the calves.

FIG. 13.—Papulo-necrotic tuberculides on the thigh, showing the central areas of scabbing necrosis.

be considered as the likeliest cause and, even if general examination, including radiography of the chest, fails to reveal a focus, the patient should be kept under periodic review for the next two years. The Mantoux reaction is likely to be positive in a dilution of 1 in 10,000.

Erythema induratum (Bazin's disease, tuberculosis indurativa, tuberculous gumma) is a hypodermal vasculitis, believed to be allergic and ending in thrombosis, fat necrosis and irregular areas of depressed atrophic scarring or ulceration (fig. 12). It is almost peculiar to young women with perniotic calves and must be distinguished from simple perniosis which is not indurated but may ulcerate as a result of vascular stasis and thrombosis. The Whitfield type of erythema induratum also has to be differentiated. This usually occurs in older women, the nodules are smaller and more widely scattered over the legs and the course is intermittent. It is a non-tuberculous hypodermal vasculitis of unknown cause. Tuberculous erythema induratum usually responds well to isoniazid or to combined treatment with isoniazid and PAS or streptomycin. Calciferol is contraindicated as it may cause a violent exacerbation with extensive ulceration.

Papulo-necrotic tuberculides erupt usually on the limbs as shotty papules

and nodules, symmetrically disposed and proceeding to scabbing, ulceration and scarring, or directly to atrophic scarring (fig. 13). The lesions erupt in crops with intervening remissions. Search should be made for an active focus of tuberculosis elsewhere and the patient treated accordingly. The lesions may then finally resolve.

Lichen scrofulosorum is a rare tuberculide occurring in children with tuberculous lymphadenitis. The eruption is non-itchy, usually confined to the trunk and consists of pale brown lichenoid papules, perhaps slightly scaly. Treatment is of the underlying tuberculous condition.

CONDITIONS OF DOUBTFULLY TUBERCULOUS ETIOLOGY

Lupus miliaris faciei, acne agminata and the rosaceous tuberculide of Lewandowsky are facial eruptions which have been attributed to tuberculosis largely because they have a tuberculoid type of histology. Their non-responsiveness to isoniazid and the absence of tuberculous foci elsewhere or of Mantoux sensitivity in high dilution suggest that they are in fact not tuberculides. It cannot be emphasized too strongly that a tuberculoid histological picture does not necessarily indicate tuberculosis. A variety of bacteria, fungi, parasites, organic and inorganic agents can produce a granuloma consisting of tubercle formation with or without caseation (Weed, McDonald and Needham, 1956).

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ANTIBIOTICS IN DERMATOLOGY

By G. B. MITCHELL-HEGGS, O.B.E., T.D., M.D., F.R.C.P.
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INFECTIONS of the skin are common and their easily visible morphology distressing, so that the inclination to resort to antibiotic therapy, be it topical or systemic, is very strong. It would therefore seem justifiable to start this short article with the well-worn plea for the rational use of the antibiotics in dermatology. The treatment of minor skin infections with the powerful wide-spectrum antibiotics is not only unnecessary but is also a disservice to medical therapeutics generally.

The development of resistance to the antibiotics, especially of the *Staphylococcus aureus*, is now of major importance in most branches of medicine and surgery and especially so in hospital practice. At the moment the production of new antibiotics would appear to be keeping pace with this and it is therefore doubly important that indiscriminate use of these life-saving drugs should be avoided in the day-to-day treatment of skin disease. It is equally true to say that the course and prognosis of many skin conditions have been altered with the advent of the antibiotics. We are now able to cut short the spread of infective eczematoid dermatitis and also to prevent the development of chronic lymphœdema resulting from repeated attacks of cellulitis. The young child is protected from the risk, small though it may be, of renal damage from repeated attacks of cutaneous infection. Thanks to insecticides and public health measures, infestation is less frequent, its sequel, impetigo, less common. Antibiotics have made this a much shorter and less serious disorder. The importance of the 'chronic infective focus' is still uncertain but it would seem likely that it plays a part in the development of certain dermatoses and perhaps in the persistence of larger groups of chronic cutaneous maladies. In the eradication of this focus, the antibiotics play a decisive part.

It is important that an infected lesion should not be allowed to persist on the skin. Many sufferers from chronic eczema, be this due to a constitutional predisposition or not, have started off with an inadequately treated break in the skin which has become infected, or alternatively, through the additional hazard of dermatitis medicamentosa from misguided, over-zealous attempts at cure.

RESISTANCE OF THE SKIN TO INFECTION

It is well known that organisms cannot enter the intact skin except by way of the pilosebaceous follicle or sweat-gland pore. In addition, we have the 'acid mantle' which, if undisturbed, may control any resident organisms. Of recent years attention has also been drawn to the self-sterilizing power of the skin, due to the combined effect of the unsaturated fatty acids and the major factor of drying. Even under optimum conditions for self-sterilization,

many pathogens may persist for several hours, especially *Staphylococcus aureus*, which may do so for several days. The validity of the evidence available, however, has been questioned by a number of authors (e.g. Pillsbury and Rebell, 1952).

Friction, whether it be secondary to pruritus or not, will damage the skin and lower its resistance to infection: e.g. boils developing in the collar area of the neck. Numerous skin diseases are associated with pruritus of variable degree and thus the possibilities of secondary infection developing are legion. Once an eczematous condition develops, and this may be due to many exogenous and endogenous factors, serous exudate appears which can prove to be a very efficient antagonist of the skin's self-sterilizing power.

The greasy skin of the seborrhœic individual is especially liable to infection. Excessive sweating, whether constitutional or environmental, will again modify the skin barrier by maceration and, if prolonged, will lead to invasion by various organisms.

Skin hazards in the home and industry are increasing daily and, although this article is concerned essentially with the antibiotic therapy of skin infections, it should be remembered that prevention is of prime importance. Once the normal equilibrium of the skin is disturbed, with or without secondary invading organisms, a chronic eczematous process may develop, the course of which is unpredictable and often protracted. Washing of the skin in waters reputed to have healing powers, or the use of lotions designed to remove the suspected 'uncleanness', has been known since Biblical times. Ever since micro-organisms and their sometimes harmful effects on the skin were discovered, the search has gone on for an agent which would have a destructive power on these organisms without damaging the skin. Lister developed the first of these agents, namely the antiseptics, leading on to the use of hypertonic saline by Almroth Wright and thence to Fleming's discovery of penicillin and the initiation of the antibiotic era. At last the problem of antibacterial treatment seemed to be solved. New problems arose, however, to replace the old.

The healthy skin is conducting a ceaseless battle against bacteria, viruses, yeasts, monilia and the like. Along with its many other powers, the skin also possesses bacteriostatic functions, a fact which has been recognized for many years. The tears have a similar protective action over the cornea and conjunctival mucous membranes. Protection may also be available through the mucous membranes of the genitalia. A great variety of organisms is to be found on the skin: staphylococci, streptococci, micrococci, *Pseudomonas pyocyanea*, monilia, fungi, viruses, and the like. The persistence of these organisms depends upon various factors; it is a well-known fact that *Pseudomonas pyocyanea* will disappear from the dry skin, remaining as long as the skin is kept wet, whereas *Streptococcus pyogenes* is affected by unsaturated fatty acids. Wear and tear of the skin are two quite different things: simple wear tends to lead to thickening or hyperkeratosis, whilst tearing or breaking the skin may encourage acute or chronic infection.

VARIABILITY OF SKIN RESISTANCE TO INFECTION

The resistance of the skin is a variable factor and may be altered in many ways. At puberty there seems to be a lowered resistance to staphylococci with a resulting tendency to furunculosis. In old age the normal changes in the skin are loss of subcutaneous fat, atrophy of the epidermis, collagen changes in the dermis, and changes in sebaceous gland activity. Senile pruritus is common but, in spite of intense scratching, there is often little damage or infection unless infestation or eczematization is an additional feature. Alterations in the humidity also affect resistance on the one hand, and may encourage the growth of bacteria, monilia or fungi on the other. Infections produced by fungi and yeasts are thus more common in humid climates. They may remain quiescent in a temperate zone to become more active with an increase of temperature. If the body is kept warmer than usual, as when the patient is confined to bed for a long period, there may be an increase in activity of mycotic infection of the feet or intertriginous areas. Changes in metabolism may indirectly encourage such growth. Sudden gain in weight may increase the tendency to sweat, and this in turn encourage the development of intertrigo. The speed with which the diabetic may develop boils, sometimes near the urinary orifices but also at distant points such as neck and limbs, has been recognized for many years. Stress, whether it be sudden shock, constant fatigue, persistent tendency to worry, or premenstrual tension, may also affect immunity and be associated with boils, herpes zoster or recurrent herpes simplex.

Resistance may, of course, be altered also by external factors which include too vigorous washing or the application of substances which may immediately or gradually wear down the skin's resistance. This is most important in industry. Recently it has been shown that the initial treatment of minor injuries in industry may be in some ways related to the development of dermatitis. In a review of 250 patients seen over the course of eight years, suffering from dermatitis arising from their employment in the steel industry, 34.8 per cent. of cases were incapacitated by dermatitis developing directly as a result of treatment of a trivial injury such as a superficial burn or small cut (Vickers, 1958).

GENERAL CONSIDERATIONS

Knowing that immunity can occur, we have to tread very cautiously when considering the use of antibiotics in any skin disorders. The indiscriminate use of the antibiotics in dermatology may lead to a further increase in the number of resistant strains of various organisms. The mechanism of resistance-development is known in the case of certain drugs, notably the sulphonamides, but is still obscure in others. It is obvious that the more antibiotics are used, the greater becomes the problem of resistance. Naturally, in common with most other branches of medicine, the use of antibiotics in dermatology today is frequent and it is therefore important to review the indications and dangers of such use. For the purposes of this article, such a

review is confined to a study of the dermatological aspects. Remembering that the word antibiotic implies the capacity for inhibiting and even destroying other micro-organisms (Waksman, 1956), the use of these drugs would usually be in those disorders in which there is an infective etiology. There are, however, one or two apparent exceptions.

Many antibiotics have been manufactured since the discovery of penicillin, and many have a wide range of bacteriostatic or bactericidal powers, i.e. the broad-spectrum antibiotics, and these may be indicated in the treatment of patients in whom penicillin has failed or in whom sensitization to it has developed. Even with routine skin testing (by patch or intradermal tests) it is not always possible to be certain if sensitization has developed and when or how it will become manifest. The skin's tendency to sensitization is so capricious that the offending agent may even be the inert base carrying the antibiotic. Thus, antibiotics should only be used when it is clear that assistance is needed urgently to combat an infection. If such infection is likely to occur, as in abrasions, ulcerations and so on, associated with severe accidents, a course of systemic antibiotic would be better as a prophylactic than dusting powder or ointment. In most cases, simple infection requires no antiseptic or antibiotic therapy. Removal of foreign bodies, followed by a dry dressing, may be all that is needed. When the infection is chronic or the course complicated, correct treatment may involve not only the appropriate antibiotic but also a spell away from work.

CHOICE OF ANTIBIOTIC

If the use of an antibiotic is under review, there are various points which should be considered before the drug is started. The possible duration of treatment with all its implications including that of sensitization and alteration in immunity should be borne in mind. Routine bacteriological confirmation of the presence of the organism and its specific antibiotic sensitivity, should be carried out for the 'ill' patient during hospital treatment, and whenever practicable in general practice. The decision should then be made between systemic and local administration. Once the choice for systemic therapy has been made, penicillin should be considered first, although any previous history of sensitization reactions, however small, will contra-indicate its use. In addition, the causal organism may well be insensitive, especially if it is a staphylococcus. It is important to remember, however, that desensitization is still possible when needed although, with the ever-increasing number of antibiotics, this need is not now so great as it was in the early days of penicillin therapy. O'Donovan and Klorfajn (1946) described attempts to desensitize a patient with subcutaneous injections of the drug; although this failed, they succeeded with slowly increasing doses given orally. Frankland (1950) found that weekly visits for treatment for at least three months were necessary for desensitization.

It may be necessary and therefore more practicable to resort to the group of wide-spectrum antibiotics which include chlortetracycline ('aureomycin'),

oxytetracycline ('terramycin'), tetracycline ('achromycin'), chloramphenicol ('chloromycetin'), and streptomycin. Although the chances of dangerous toxic effects from chloramphenicol are slight, it would seem reasonable to choose this drug with great care. In the case of streptomycin, resistant strains are more likely to develop, sometimes with remarkable rapidity, and sensitization reactions are more common than with the other members of the group. In addition, streptomycin has a vital part to play in anti-tuberculous therapy. Erythromycin should be kept in reserve for the exceptional case in which the organism is insensitive to other antibiotics. Provided the organism is sensitive, I prefer to use tetracycline, chlortetracycline or oxytetracycline. As in other fields, drugs used in dermatological cases should be administered for a minimum of five days in the usual dosage.

FIG. 1.—Infective eczematoid dermatitis. (*By courtesy of Dr. R. M. B. MacKenna*)

If topical application is required, penicillin, chloramphenicol and streptomycin should be used with the greatest care, because of their marked propensity to produce epidermal sensitivity. Chlortetracycline (0.5 to 1 per cent. in a cream or ointment base is usually all that is required) is very effective, and so is oxytetracycline. It is preferable, however, to use as first choice a substance that is not used systemically, such as neomycin, bacitracin or soframycin. These substances do not sensitize easily, and are effective in their action.

Unfortunately, prolonged systemic use of antibiotics will bring about a rapid increase in resistant organisms and monilia, and more cutaneous moniliasis is now seen. This is sometimes of great significance in pruritus ani after the use of life-saving antibiotics. If local therapy is not having the desired effect, it should be stopped after a week or so. It should be remembered that antibiotic therapy alone is often not enough. In the first instance, it should be used with older tried remedies, and in the second, antibiotics may be used in combination when one type alone would be ineffective. This has led to a certain amount of indiscriminate mixing, however, so that in certain cases, strains originally resistant to one of the components, have been

stimulated by the new combination. Thirdly, antibiotics may be combined with steroids. In conditions such as infected skin disorders, in which the etiology may be difficult to determine, the use of combined steroid and antibiotic therapy is of the greatest benefit. The steroid will combat pruritus

FIG. 2.—Lymphœdema: Before (a) and after (b) antibiotic treatment.

and inflammation, whilst the antibiotic will halt any infective process. Such a combination is indicated in intertrigo, otitis externa, infective eczematoid dermatitis and any secondarily infected disorders. Although it is impossible for one individual to do clinical trials on all the preparations available, I have been impressed by the value of 'cortibiotic' (Roussel), 'neomagnacort' (Pfizer) and 'terracortril' (Pfizer).

INDICATIONS FOR THE USE OF ANTIBIOTICS IN DERMATOLOGY

Persistent skin infection which in itself, or through local treatment, may lead to the development of sensitization. This is most commonly seen round the ears and sides of the neck, often starting as retro-auricular fissuring, passing on to the stage of infective eczematoid dermatitis (fig. 1). In many instances, the severity of the eczematous reaction is such that the skin will tolerate only bland local applications; thus, if antibiotic therapy is required, it is often necessary to use systemic administration. Alternatively, a combination of hydrocortisone and an antibiotic may be used topically.

Impetigo, ecthyma and pemphigus neonatorum.—Impetigo is usually adequately controlled without antibiotic therapy, alternatives including 'quinolor compound ointment' or 'propamidine cream' (Mitchell-Heggs and Mitchell-Heggs, 1950), but neomycin or bacitracin may be required. Ecthyma, often streptococcal in type, usually requires the use of an antibiotic, either topically or systemically and can prove resistant to treatment. Pemphigus neonatorum is simply a widespread bullous impetigo due to *Staphylococcus aureus* occurring in the first few weeks of life, and usually requires systemic antibiotic therapy.

Erysipelas and cellulitis.—Recurrent attacks of cellulitis, usually resulting from fissuring of the skin, e.g. retro-auricular or interdigital, may lead to chronic lymphœdema (fig. 2), and should be controlled as soon as possible so as to prevent permanent deformity.

Boils and carbuncles.—In many instances of recurrent boils and carbuncles, it is not possible to control the condition with the topical antibiotics of choice, and an attempt must be made with systemic therapy to sterilize the skin of the entire body while clearing the active infection. This ideal is often difficult to attain because of chronic foci of infection such as nasal vestibulitis and other indeterminate factors, including variations in immunity reaction, individual skin resistance, general health.

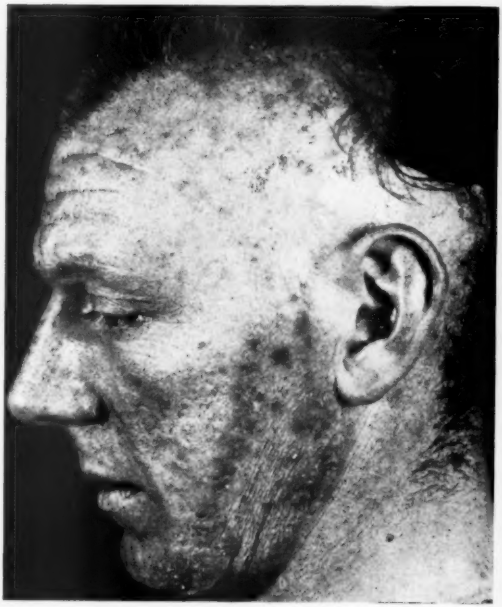

FIG. 3.—Lupoid sycosis barbae. (*By courtesy of Dr. A. Porter*)

Folliculitis (*Bockhart*), *folliculitis barbæ and sycosis barbæ.* — Sycosis barbæ (fig. 3) is a chronic infective process leading to scar formation and spreading with peripheral activity over the beard area and sometimes even into the scalp leaving a trail of permanent scarring alopecia. The antibiotics should be tried but are often only of temporary help.

Hidradenitis suppurativa.—In hidradenitis suppurativa (fig. 4) infection of the apocrine glands occurs, most commonly in the axillæ. Once the condition takes a hold it is very resistant to treatment and it is therefore justifiable to treat all cases of axillary folliculitis and boils with systemic administration of the appropriate antibiotic as a prophylactic measure.

Acne vulgaris.—In acne vulgaris, opinions are divided as to the justification for the use of antibiotic therapy. The acne pustule is usually sterile but secondary invasion with pyogenic organisms does occur and in the very persistent and chronic case some temporary relief may ensue from their use.

Tuberculosis cutis.—Lupus vulgaris is usually well controlled with a combination of isoniazid and PAS without the necessity of resorting to the more powerful and toxic drug, streptomycin. A few of the so-called tubercu-

lides, especially erythema induratum (Bazin), may be similarly improved.

Stasis ulcer.—In stasis ulceration it is likely that infection plays only a minor part in a condition which results in the main from the effects of hypostasis. The topical application of antibiotics, if used for a long time, is liable to produce an eczematous reaction or aggravate the commonly existing stasis eczema. Stress should be laid on the adequate use of supportive bandages, physiotherapy and surgical treatment of incompetent veins.

FIG. 4.—Hidradenitis suppurativa.

Otitis externa.—This is essentially an eczematous process with secondary infection and as such may well lead to recurrent attacks of cellulitis and chronic lymphœdema with gradual closure of the external auditory canal. The combined topical application of an antibiotic and hydrocortisone for short periods of time has revolutionized the treatment of this previously very resistant and chronic malady.

Paronychia.—Chronic paronychia is usually little affected by antibiotics, as it is essentially a chronic inflammation of the skin surrounding the nail, perpetuated by minor trauma and exposure to wet. The antibiotics may play some part, however, in the treatment of the very early stages. The significance of the constant isolation of monilia in this condition is still uncertain.

Pustular bacterid.—In this condition, which is characterized by flares of pustules on the palms and soles, the antibiotics may be of assistance with the individual attacks but search should be made for a focus of chronic infection.

Pemphigus.—The pemphigus group of eruptions is now adequately controlled by steroid therapy, although the use of penicillin occasionally leads to encouraging improvement, and even today, penicillin or its more modern successors are well worth a trial in cases in which there is heavy bacterial involvement of the skin.

Acrodermatitis atrophicans of Herxheimer.—For a long time no cure was known for this disorder; today, parenteral use of penicillin is the treatment of choice.

Lichen planus.—Occasionally, lichen planus has been helped by courses of penicillin.

CUTANEOUS SIGNS OF ANTIBIOTIC INTOLERANCE

Hypersensitivity reactions occur most commonly with the administration of penicillin, and are said to develop in 1 to 5 per cent. of patients treated with this drug. In the early days of penicillin therapy, indiscriminate use of topical

penicillin led to the frequent development of epidermal sensitivity, presenting as acute contact eczema. In systemic therapy the immediate reaction takes the form of acute anaphylaxis and may prove fatal. The delayed reaction, which appears from twenty-four hours to four weeks after administration of the drug, is variable but usually takes the form of serum sickness, which includes pruritus and urticaria. Thus, penicillin sensitivity may trigger off a chronic urticaria of many months' duration. Streptomycin should rarely, if ever, be used topically, because of its marked tendency to produce epidermal sensitivity. Chloramphenicol also not infrequently produces a similar contact eczema. The other wide-spectrum antibiotics rarely produce dermal or epidermal sensitivity.

It is well known that the skin is limited in its morphological patterns of reaction and these patterns therefore are common to the antibiotics as a group. With the development of hypersensitivity a variable number of cutaneous eruptions may occur ranging from simple pruritus and erythema, through a combination of erythematous macules, papules or morbilliform eruption, to a generalized exfoliative dermatitis.

CONCLUSION

(1) Be sure the antibiotic is really needed.
(2) Be sure to use one which will not endanger the patient's life or skin.
(3) Be sure to use an adequate dose.
(4) Be alert for complications.
(5) Finally, tell the patient if he is hypersensitive and make sure that this information is readily available for those who might treat him after you.

I wish to thank Dr. W. Frain-Bell for help in completing this article. The photographs were taken by Mr. R. Lunnon of the Institute of Dermatology, and reproduced by kind permission of the Dean, Dr. F. Ray Bettley.

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VITAMINS AND THE SKIN

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ADEQUATE nutrition is essential for the preservation of a healthy skin just as it is essential for the maintenance of a healthy body. So it is not surprising that the skin is one of the first and major sites in which vitamin deficiencies manifest themselves. Proper nutrition is, of course, dependent not only upon an adequate supply of vitamins but also upon other essential food factors such as proteins and fats. It should also be pointed out that very often under actual conditions one deals with a deficiency of more than a single vitamin and that it is this combination of deficiencies which causes the clinical manifestations.

Vitamin deficiencies in the skin are due either to an insufficient supply of vitamins at the site of absorption in the gastro-intestinal tract (and in the case of vitamin D in the skin) or to the inability of the gastro-intestinal tract to absorb vitamins, even though the supply is adequate. For example, in macrocytic anæmias the major defect may lie in faulty absorption rather than in a poor supply. In still other instances, the skin itself may be unable to utilize an otherwise sufficient quantity of vitamins or to convert them into forms which can be further metabolized. Here the possibility must be considered that the individual or his skin may require a higher level for vitamins or for a specific vitamin than that which is generally accepted by nutrition experts as 'normal'. In some patients such unusually high requirements for vitamins appear to be due to a metabolic peculiarity or the result of infection, pregnancy, or a systemic disease. Still another condition which may account for avitaminoses but which thus far has received little attention is the role of the vitamin competitors. One has only to think of the folic acid antagonist, aminopterin; the nicotinic acid antagonists, isoniazid and sulphapyridine; the riboflavine antagonist, isoriboflavine; the thiamine antagonist, pyrithiamine; and the pyridoxine antagonist, 4-desoxypyridoxine, to realize that such vitamin competitors can be synthetized. There seems, however, to be limited knowledge concerning the natural occurrence of such competitors in food and especially in the form of additives in modern 'prepared' foods and in drugs.

CUTANEOUS MANIFESTATIONS OF AVITAMINOSES

The cutaneous effects of *vitamin A* deficiency are based mainly on the lack of the anti-keratinizing action which is normally exerted by this vitamin.

Characteristic changes of vitamin A deficiency in the skin occur first on the extensor surfaces of the arms and thighs and the flexor surfaces of the legs and appear in the form of papular lesions, located at the pilosebaceous follicles. The resulting eruption may resemble goose-flesh or a nutmeg grater, and the clinical picture is highly reminiscent of such non-avitaminotic eruptions as keratosis pilaris, lichen pilaris, lichen spinulosus or ichthyosis follicularis. The skin of patients suffering from vitamin A deficiency generally tends to be dry, scaly and crinkled, and sometimes has the fishskin-like appearance of ichthyosis. Comedone formation is still another feature described in vitamin A deficiency. The comedones, however, are situated on an excessively dry skin in contradistinction to the very oily skin which forms their terrain in acne vulgaris.

Sjögren's syndrome, which also has been attributed to vitamin A deficiency, is associated with severe dryness of the mucous membranes due to inadequate secretion from the salivary, lacrimal and respiratory mucous glands. These disturbances lead to keratoconjunctivitis, dysphagia, hoarseness and loss of sense of taste and smell. We have seen no significant change in this syndrome after intensive and prolonged treatment with vitamin A and it therefore seems to us that there is insufficient evidence thus far to prove that Sjögren's syndrome is produced by a deficiency in vitamin A.

The sites of predilection for the cutaneous changes of *pellagra* are those skin areas which are most exposed to trauma such as sunlight, heat, pressure and friction. Sunlight is by far the most important of these factors since a true photosensitization appears to be evident in this disease. The lesions are symmetrically distributed over the light-exposed areas, with the butterfly area of the face a common site. The early changes resemble sunburn; later there are well-defined large macules of light or dark red hue and bullæ, as well as crusting and desquamation. In chronic cases the skin becomes thickened, roughened, scaly and pigmented. Follicular plugging, atrophy of the skin and ecchymoses may also occur. The mucous membrane alterations are prominent. The tongue may be œdematous, denuded and scarlet red in severe acute deficiency, and beefy red in chronic deficiency. These changes are associated with burning of the mouth and tongue which sometimes extends into the pharynx and œsophagus. Ulcers resembling those of aphthous stomatitis may be seen. The papillæ of the tongue are hypertrophied at first and later become flattened, atrophied and fused. Eventually a cobblestone pattern develops and finally there is a shiny and atrophic appearance.

'*Kwashiorkor*', the South African name for a form of infantile pellagra, may be rapidly fatal unless treatment is instituted. Among the cutaneous diagnostic features of this disease are curliness and depigmentation of the hair, alopecia, reddish-brown pigmentation of the face with circumoral depigmentation and a depigmented, reddish, oozing eruption with cracking, on the extensor surfaces of the extremities, the so-called 'crazy pavement' dermatosis. This type of nutritional deficiency is not limited to South

African children and has been observed in other areas where famine, starvation or inadequate diet exists. It is relieved by a high-protein diet.

Riboflavine deficiency presents characteristic cutaneous and mucous membrane changes. Here one may see cheilosis with reddening, thinning, scaling, chapping and wrinkling of the lips as well as angular stomatitis with erythema and fissuring, the so-called perlèche. Purplish discoloration, œdema and flattening of the filiform papillæ produce the picture of the 'magenta' tongue. Greasy scaling and erythema occur in the areas of the ala nasi, canthi, pinnæ and other folds of the skin and there is coarsening and elevation of the sebaceous follicles of the nose and cheeks. Severe scrotal dermatitis has also been described.

Certain cutaneous features due to deficiency in other vitamin B complex factors have been described in animals, but there is a dearth of reliable evidence that similar avitaminotic changes occur in the skin of man. Vitamin deficiencies which have been observed in laboratory animals, but which thus far have not been shown to cause cutaneous manifestations in man, are alopecia and greying of the hair in rats produced by pantothenic acid deficiency and a seborrhœic dermatitis-like eruption in rats produced by biotin deficiency. Biotin deficiency in man has been experimentally produced but there is no convincing proof that it occurs naturally.

The early phases of cutaneous manifestations of *ascorbic acid* deficiency consist of hyperkeratotic follicular papules on the buttocks and calves, which may be very reminiscent of the cutaneous lesions attributed to vitamin A deficiency. As the condition progresses, however, the well-known hæmorrhagic tendency of scurvy, with petechiæ and ecchymoses, develops. This can easily be demonstrated with the Rumpel-Leede test. Furthermore, the skin is pale because of the associated anæmia. Mucous-membrane involvement is evident with swelling, erythema and bleeding of the gums.

Avitaminosis K also results in a hæmorrhagic tendency because of the abnormal lengthening of the prothrombin time. This leads to extensive purpura in the skin.

Treatment of these true deficiency states associated with cutaneous manifestations consists in the administration of appropriate vitamins in adequate doses, simultaneously with a nutritionally adequate diet over sufficiently long periods of time. Generally, the time required for such treatment to produce clinically apparent improvement is from a few days to several weeks, in contradistinction to the treatment of non-avitaminotic dermatoses in which high doses of vitamins often have to be given for many months before the therapeutic result becomes noticeable.

THE USE OF VITAMINS IN OTHER DERMATOLOGICAL CONDITIONS

There are many dermatological conditions for which vitamin therapy has been recommended besides these generally recognized cutaneous manifestations of avitaminoses. Such therapy has often been suggested even though

its proponents have known that there was no existing deficiency. The basis on which vitamin therapy has been attempted in these circumstances has at times been the clinical resemblance, real or imagined, between the presenting signs of these dermatoses and recognized avitaminoses. Theoretical considerations or pure empiricism have been the reasons for therapeutic trials with vitamin therapy in some other dermatoses. In these non-avitaminotic dermatoses, vitamins are often used as drugs rather than as essential nutritional factors; this is evident not only from the absence of signs or symptoms of avitaminosis but also from the very large, sometimes fantastic, quantities of vitamins administered. We shall mention only those dermatoses where in our own experience vitamin therapy proved to be of benefit or failed.

VITAMIN A

Very high doses of vitamin A have unquestionably been helpful in some cases of pityriasis rubra pilaris and keratosis follicularis (Darier's disease). Both of these rather uncommon dermatoses are associated with keratotic papular lesions which remotely resemble the follicular keratotic papules of avitaminosis A, and it is these lesions which often regress under vitamin A treatment. The suggested dose of 100,000 to 200,000 units daily must be maintained over a period of many months or years.

In ichthyosis the administration of vitamin A, even in very high doses, has been disappointing. It has been difficult to evaluate the action of vitamin A in such common cutaneous problems as keratotis pilaris, lichen spinulosus, rough, dry and scaly skin, and brittle hair and nails because these conditions often undergo fluctuations due to a variety of factors, such as climate and seasons, which cannot be controlled. It has been our distinct impression, however, that vitamin A has produced improvement in some cases and is therefore worth a trial in keratosis pilaris, lichen spinulosus and dry skin. Our results with vitamin A in brittle nails have been disappointing but the results achieved in this condition with daily oral administration of gelatin appear to be far more successful. The best approach for the present is the combined treatment with gelatin and vitamin A.

Acne vulgaris is one of the more controversial present-day indications for vitamin A therapy. It is well known that among the principal factors which produce the typical comedone and papule of acne vulgaris is an excessive keratin ring formation which produces abnormal narrowing of the follicular opening and so prevents the escape of the large quantities of sebum secreted by a hyperactive sebaceous gland. The theoretical basis for vitamin A therapy in acne vulgaris is the assumption that its anti-keratinizing action counteracts the tendency to the formation of this obstructive keratotic ring. It is our opinion, based on many years of experience, that a trial with vitamin A, 50,000 units daily, is indicated, especially when there is a pronounced tendency to keratotic plugging at the follicular orifice together with comedone formation.

Vitamin A appears helpful also in patients with atopic dermatitis who show pronounced clinical signs and symptoms of plugging of the sweat pores, particularly when the sides of the trunk appear 'peppered' with minute skin-coloured firm papular lesions.

In all dermatoses in which vitamin A is used as adjuvant treatment rather than for relief of a vitamin deficiency state, therapy should not be abandoned as unsuccessful until it has been tried for at least three to four months. Vitamin A is not detectable in skin but it is suspected that it may be present in a 'masked' and therefore undetectable state. When applied topically to the skin of certain laboratory animals it produces thickening of the epidermis and also a suppressive action on keratin formation. Experimental work in human skin, however, has thus far failed to demonstrate a similar effect from the topical application of vitamin A. Despite this lack of experimental support creams containing vitamin A have been extensively used, especially in cutaneous conditions in which systemic vitamin A administration has proven beneficial. Here again, well-controlled clinical investigations are lacking. Our own experience suggests that creams containing vitamin A (e.g. 500,000 units per ounce [17,500 units per g.]) may be beneficial on senile dry skin and on dry skin resulting from excessive and prolonged exposure to the sun and the elements. There has been no noticeable improvement, however, from the topical application of vitamin A in keratosis pilaris, lichen spinulosus and acne vulgaris. Lozenges with a high content of vitamin A have recently been made available for local therapy of oral mucous membrane lesions such as leucoplakia and lichen planus. The experience gained thus far does not permit us to draw any conclusions regarding the value of vitamin A so administered.

THE VITAMIN B COMPLEX

The vitamin B complex and its various components, more than any other vitamin, perhaps, exclusive of vitamin A, has been given extensive trials in non-avitaminotic dermatoses. Especially in seborrhœa and seborrhœic dermatitis, vitamin B complex, nicotinic acid, riboflavine, biotin and pyridoxine in large doses have been intensively investigated. This is mainly due to the fact that one can produce seborrhœic dermatitis-like eruptions in laboratory animals on vitamin B deficient diets. Our own experience in seborrhœic dermatitis has been consistently disappointing and we are of the opinion that vitamin B therapy is not indicated in the routine management of this disease. We are also unimpressed by the results of vitamin B complex therapy in psoriasis. In acne rosacea, however, treatment with vitamin B complex and nicotinic acid does appear to be helpful, especially in patients in whom alcoholism is a contributory factor. Nicotinic acid has been used successfully in exceptional cases of dermatitis herpetiformis. Its efficacy in this disease has been attributed to the pyridine ring contained in its molecule, rather than to a vitamin effect.

In recent years vitamin B complex has often been given to forestall

monilial and other complications of therapy with broad-spectrum antibiotics. The assumption has been made that the disturbance in the ecological balance produced by these drugs leads to a deficiency in those vitamins (e.g. nicotinic acid) which the human body, in part at least, derives from micro-organisms which physiologically inhabit the gastro-intestinal tract. This iatrogenic hypovitaminosis in turn is thought to lower the normal resistance of the muco-cutaneous tissues to the action of surviving micro-organisms, especially *Monilia albicans*. To our knowledge there are no well-controlled clinical investigations which conclusively prove that patients under combined treatment with antibiotics and vitamin B complex as a group develop less muco-cutaneous complications than patients who receive the antibiotics without vitamin B complex, but it would appear wise to reserve judgment until such time as the results of controlled studies are made available. In our experience vitamin B complex therapy has failed in non-avitaminotic cases of perlèche, stomatitis, glossitis and burning tongue.

Aneurine chloride by subcutaneous injection and by mouth has been used with apparent benefit in treating some patients with neuralgia of herpes zoster. Here again evaluation of therapeutic effects has been difficult because the pain tends to disappear spontaneously during the first few weeks after onset, especially in the young and middle aged.

Pantothenic acid is said to have benefited cases of chronic discoid lupus erythematosus. Whilst we cannot report such results in a small number of our patients so treated, a recent report, which suggests that there is a disturbance in the ratio of free and bound whole blood pantothenic acid levels in both chronic discoid and acute disseminated lupus erythematosus, makes further investigation of the role of pantothenic acid in this disease desirable.

Spontaneously occurring biotin deficiency has not been observed in man, but feeding of dehydrated egg-white to human volunteers has produced scaling and a greyish discoloration of the skin, as well as atrophy of the lingual papillæ. It has been repeatedly suggested that biotin be used for treatment of seborrhœic dermatitis, but the results generally appear to have been disappointing. From time to time good therapeutic effects from biotin have been claimed in infants with seborrhœic dermatitis and Leiner's disease.

VITAMINS C, D, E, F, AND K

Vitamin C therapy has been recommended for such diverse diseases as atopic dermatitis, allergic contact dermatitis, psoriasis and non-avitaminotic hæmorrhagic lesions. In none of these have we seen any benefit from administration of this vitamin.

Vitamin D_2 was widely and successfully used some years ago in the treatment of lupus vulgaris and certain other forms of tuberculosis of the skin. In more recent years, however, it has been almost completely replaced by streptomycin, isoniazid and para-aminosalicylic acid.

We know of no dermatoses in which treatment with *vitamins E, F or K* has proven of value.

CUTANEOUS SIDE-EFFECTS OF VITAMIN THERAPY

A number of cutaneous side-effects due to therapeutic administration of vitamins in deficiency states or in various non-avitaminotic dermatoses has been reported by reliable investigators. Chief among these are allergic manifestations which have been noted after the administration of certain vitamins. Aneurine chloride, for example, has caused urticaria, angioneurotic œdema, generalized itching, and contact dermatitis. Nicotinic acid has been reported to have engendered contact dermatitis and anaphylactic shock. Vitamin B_{12} (cyanocobalamin), which contains cobalt, is said to be capable of causing reactions in cobalt-sensitive and even perhaps in nickel-sensitive persons. A maculo-papular pruritic eruption resulting from administration of folic acid has been described.

Certain modern vitamin preparations, so-called 'dietary supplements', which contain combinations of many of the known essential vitamin factors and minerals, are another source of undesirable cutaneous effects. We have seen occasional cases in which the iodides which are among the minerals in these preparations have caused typical iodide eruptions or have produced a flare-up of dermatoses such as acne vulgaris, acneiform eruptions and dermatitis herpetiformis which are known to be made worse by iodides.

The administration of excessive quantities of most vitamins apparently does not produce cutaneous manifestations of hypervitaminosis. Excessive doses of vitamin A, which have been reliably shown to lead to potentially serious side-effects, especially in children, are an exception to this. The cutaneous manifestations of hypervitaminosis A are itching, rough and scaly skin, perlèche, night sweats, hair loss and brittleness of the nails. The interesting fact will be immediately recognized that these cutaneous difficulties are very similar to those states for which the therapeutic administration of vitamin A in moderate doses has been recommended and found beneficial.

SUMMARY

Among the various possible causes of vitamin deficiencies are inadequate nutrition, faulty absorption, faulty utilization, abnormally high metabolic requirement and the effects of vitamin competitors.

The different vitamin deficiencies which may cause pathological alterations specifically in the skin are described.

Vitamins have also been used extensively in cutaneous conditions in which no detectable deficiency state exists. In most of these non-avitaminotic dermatoses the early claims for therapeutic results with vitamin therapy are not yet substantiated.

Some of the dermatoses in which vitamin therapy has been found effective or worth a trial are discussed.

The fact that very large doses of vitamins have to be administered over a protracted period of time also suggests that the therapeutic effect here is based on a drug-like action rather than on substitution for deficient vitamins.

SOME CLINICAL ASPECTS OF RESEARCH ON SEBUM AND THE SEBACEOUS GLANDS

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It is obvious that to comprehend the abnormalities known as seborrhœa and acne vulgaris, the complex activities of the sebaceous glands must be fully understood. Similarly, if the many problems concerning the etiology and pathology of certain cutaneous diseases, particularly seborrhœic dermatitis, are to be solved, a study of sebaceous activity is of great importance. During the past decade many investigations of sebaceous activity have been undertaken by a variety of workers and the results of their investigations are beginning to form a coherent picture. It is the purpose of this article to summarize these investigations and to show how they are going to help the clinician of the future. At the onset it seems desirable to state that, although seborrhœic dermatitis is certainly related to sebaceous gland activity, there is as yet no scientific proof of this.

THE NATURE OF SEBUM SECRETION IN NORMAL SUBJECTS

The sebaceous glands, first described in detail by Eichorn in 1826, are present in all mammalian skin. In most areas they are appendages of the outer root sheath of the hair follicles and open to the surface of the skin by way of the pilosebaceous canals. The glands are holocrine, the gland cells disintegrating to form the sebum secreted. Sebum is largely composed of lipids, but contains some cellular debris and proteinous material. Once secreted on to the skin surface, the sebum remains there until it is removed by contact with clothing or by washing. The amount of sebum on the skin surface at a given time can be used as a rough index of the activity of the sebaceous glands in that particular area of skin. Many studies have been made involving measurements of this so-called 'sebum level'; these have been reviewed by Hodgson-Jones, MacKenna and Wheatley (1952).

Wide individual variations occur in the sebum level of a given area of the body, but there is a definite gradation in the sebum levels of different areas, the highest occurring on the scalp and the lowest on the extremities. Certain areas, e.g. the palms of the hands and the soles of the feet, have no sebaceous glands of their own but derive their layer of sebum from adjacent areas, either by direct contact or by the sebum flowing over the moist skin.

A variety of factors has been found to regulate sebaceous activity. There is no evidence of direct nervous control but there is considerable evidence

of the effects of hormones. Androgens cause a marked stimulation of sebaceous activity and progesterone appears to have a similar though less marked effect. Œstrogens, on the other hand, depress the activity of the sebaceous glands and, when administered to animals in large doses, can cause the glands to atrophy. Castration will also cause a diminution in the secretion of sebum. The effect of hormones is well illustrated by the marked sebaceous changes during the normal menstrual cycle of women. The sebum secretion rises steadily until the twelfth to fifteenth day of the cycle, then remains steady until the onset of menstruation when it falls sharply. It has long been realized that diet can influence sebaceous secretion and the subject has been well reviewed by Rothman (1954). Excessive ingestion of fats and also of carbohydrates appears to increase sebaceous secretion, but this subject requires fuller investigation. It is believed that nutritional deficiencies, particularly of riboflavine, may cause damage to the sebaceous apparatus but this again requires confirmation. Sebaceous secretion is much lower in children than in adults; it increases at puberty and diminishes in old age. Sebaceous gland function is markedly affected by atmospheric temperature, the glands being most active at higher temperatures, but there is no evidence that other changes in atmospheric conditions alter their activity. Emotional factors, too, appear to be able to influence sebaceous activity but the mechanism of this action is not fully understood.

CHEMICAL NATURE OF SEBUM

Human sebum is a very complex mixture; its over-all composition is roughly as follows: free fatty acids (30 per cent.), glycerides (30 per cent.), waxes (15 per cent.: esters of straight and branched-chain alcohols), cholesterol and cholesteryl esters (4 per cent.), squalene (8 per cent.), and other hydrocarbons (5 per cent.). The remaining 8 per cent. contains small amounts of various sterols including a little pro-vitamin D, oxidation products of squalene and a variety of unidentified compounds (Wheatley, 1952).

The fatty acids of sebum are of considerable interest. The first study of their nature indicated the presence of acids with an odd number of carbon atoms. Up to this time it had been thought that only acids with an even number of carbon atoms occurred naturally, and this observation was of considerable interest. More recently the presence of branched and highly branched acids has been demonstrated: in fact the pattern of fatty acids is completely different from that of any other tissue fat of the human body.

The normal straight chain fatty acids contain an unbranched carbon chain:

$$CH_3CH_2CH_2.....CH_2COOH$$

Simple branched chained acids have a single methyl side group attached to the penultimate (iso-) or antepenultimate (anteiso-) carbon atom of the chain:

$$\begin{array}{l} CH_3 \\ | \\ CH_3CH_2CH_2CH_2..CH_2COOH \end{array}$$

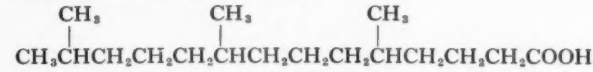
iso-acid

$$\begin{array}{l} CH_3 \\ | \\ CH_3CH_2CHCH_2CH_2..CH_2COOH \end{array}$$

anteiso-acid

The highly branched acids have an undetermined number of methyl side-groups. A

possible example of such an acid would be:—



At present our knowledge of the composition of the sebum of animals other than man is limited.

The sebum of the sheep, i.e. sheep wool or lanolin, has been studied in considerable detail, and that of common laboratory animals has also been studied. Analyses have been made of ox sebum, the preen gland secretion of certain birds, and the sebum of the horse, dog, cat, and goat. The main feature of this work is that it indicates that the composition of sebum is different for each species of animal. The sebum of the sheep contains appreciable amounts of the trimethyl-sterols, lanosterol and related substances (often collectively referred to as 'isocholesterol'), and these substances are also found in the sebum of other ruminants. Only a minute trace of lanosterol has been detected in human sebum. Other differences are the presence of hydroxy-fatty acids in sheep sebum and the absence of squalene. Squalene is only present in appreciable amounts in horse and human sebum; it is completely absent or present only in a minute trace in other animal sebum so far examined. Rodent sebum contains appreciable amounts of the sterol lathosterol (cholest-7-en-3β-ol). In addition to these differences the pattern of fatty acids shows very marked species differences.

METHODS USED FOR THE STUDY OF SEBACEOUS ACTIVITY

There are two aspects of the study of the activity of the sebaceous glands: (a) the rate of sebaceous secretion can be measured by some suitable methods, and (b) study of the chemical composition of sebum can be made in order to assess abnormal metabolic activity of the glands. The first of these measurements is comparatively easy to determine and consists in measuring the amount of sebum covering a given area of skin, either at an arbitrary time or at a fixed interval after defatting the skin, i.e. in order to calculate the absolute rate of secretion. The casually determined sebum level (defined as the number of micrograms of sebum covering one square centimetre of skin) is an easy value to determine and is roughly proportional to the activity of that particular area of skin.

It is much more difficult to study the chemical composition of sebum, partly because of the difficulty in collecting sufficiently large samples for analysis, but mainly because of the lack of small-scale methods for the determination of the various components of sebum.

The cholesterol content of sebum is easy to measure and many studies of this particular component have been made. A limited number of studies has also been made of certain constants, e.g. the iodine number and acid number, which are also easy to determine, but only limited information can be obtained from such studies. In view of the complex nature of sebum, it is not possible to determine the over-all composition of a sample of sebum collected from one subject; nevertheless the recent introduction of gas-chromatography for the analysis of complex mixtures of fatty acids has now made it possible to determine the complete fatty acid composition of a single sample of sebum (James and Wheatley, 1956). This is a noteworthy advance for it enables an analysis to be performed on a few milligrams of material which was previously impossible with many hundreds of grammes. Such an analysis will give some indication of the general metabolic activity of the sebaceous glands.

CLINICAL STATES IN WHICH THE RATE OF SECRETION MAY BE ALTERED

A marked increase in sebaceous activity has been observed in encephalitis lethargica, but in other clinical conditions any alteration is much less marked. In acne, a definite, though small, increase in general sebaceous activity occurs, although on the affected areas the actual sebum level may be lower than normal because of the sebum failing to gain access to the surface. Increased sebum levels have been thought to occur in psoriasis but this claim has not been substantiated. In seborrhœic dermatitis there does not appear to be an increase in the activity of the sebaceous glands in spite of the usual association of the condition with seborrhœa. This latter condition of the skin appears to be assessed more from the general appearance of the skin than from actual measurements of sebaceous activity and it is difficult to make a scientific assessment of these observations.

There is some evidence that defatting of the skin increases its sensitivity and allows eczematization to occur more readily. It has therefore been proposed that the measurement of sebum levels may be of value in preventive medicine for eliminating susceptible people from occupations in which they are exposed to detergents and other defatting agents. From the clinical point of view this is possibly the only direct application of such determinations, for in skin diseases there is too small a change in the sebum level to be of diagnostic use.

CLINICAL STATES IN WHICH THE COMPOSITION OF SEBUM IS ALTERED

Earlier investigations indicated that alteration in the composition of sebum might prove more important clinically than the secretion rate of the sebaceous glands. Indeed, one of the criteria of 'la kérose of Darier' and 'the seborrhœic state' of Barber is a modification, of unknown nature, of the surface skin fat or sebum of such subjects. Exact information of such changes in chemical composition is very scanty, due, as already mentioned, to the difficulties of the chemical analysis of sebum, but some important observations have been made which can now be summarized.

Cholesterol content of sebum.—Many observations have been made of the cholesterol content of sebum. Very early it was found that the cholesterol content of children's sebum was higher than that of adults. In psoriasis, acne, and seborrhœic dermatitis, there is very little, if any, alteration in the total cholesterol content, although in psoriasis there is a definite difference in the percentage of esterified to total cholesterol, the percentage being lower than in normal controls (Rothman, 1950).

In general the cholesterol content of the surface skin fats appears to depend upon the method of collection used. The greater the chance of admixture with horny layer material the higher the cholesterol content of the resultant fat. There is also an apparent correlation between the sebum level and the cholesterol content, the lower the sebum level, the higher the cholesterol content. The cholesterol of the surface skin fats results from two sources: the sebaceous glands and the keratinizing

epidermis. Only a relatively small amount comes from the sebaceous glands, whilst a small contamination with epidermal lipids can raise the amount of cholesterol considerably. Hence the apparent higher cholesterol content of children's sebum, and the higher values recorded in the literature for sebum from subjects with much dandruff and with other conditions that cause increased keratinization.

There is some evidence that large doses of cholesterol can cause an increased concentration in the sebum, and also that there is a direct influence of the cholesterol level in blood serum. The subject has been adequately reviewed by Rothman (1954), and it is wise to view with some caution any conclusions regarding the variations of the cholesterol content of sebum.

Acne vulgaris.—Preliminary observations on the over-all composition of sebum in acne by Kile, Snyder, and Haefele (1950) failed to show any demonstrable difference from normal subjects. Later observations showed that there is a definite increase in the ketosteroid content of sebum in the acne subject (Dubovyi, 1955), an observation which may well explain the mechanism of formation of the acne comedo. Other changes in the composition of acne sebum are probably slight, although preliminary observations indicated a decrease in the unsaturated fatty acid content. This latter observation is now being thoroughly investigated.

Seborrhœic dermatitis.—Observations of the sebum from subjects with seborrhœic dermatitis showed a slight though definite difference from normal subjects (Hodgson-Jones, MacKenna, and Wheatley, 1953). Further studies are now being made of the fatty acid pattern in this condition to see if there is a definite change in the metabolic activity in the sebaceous glands. Preliminary studies indicate a defect in the formation of the unsaturated fatty acids but a large series of cases requires to be studied before definite conclusions can be drawn.

Psoriasis.—Increase in the free choline content of sebum from both seborrhœic and psoriatic patients has been observed. Unpublished results from this laboratory on the sebum from psoriatic patients showed changes similar to those observed in seborrhœic dermatitis. This suggests that these changes in the surface lipids may be associated with the keratinization process of the epidermis (Snider, Gottschalk and Rothman, 1949).

DIET AND SURFACE SKIN FATS

There is some evidence that the sebaceous glands can take up fats directly from the blood as well as elaborate their own characteristic secretion. The evidence for this is still scanty and indicates so far that this only occurs in overfed subjects. This problem is now being investigated by animal experiments.

The difficulties in the way of animal experiments in sebum studies are twofold: lack of knowledge of the chemistry of the sebum of experimental animals, and the problem of collecting frequent samples of sebum. In the case of the common laboratory animals, the first of these difficulties has now been overcome. The guinea-pig, mouse, rabbit, and rat can now be used for many studies of the metabolic activities of the sebaceous glands. In view of the wide species variations in sebum composition, they cannot be used for all such studies: for instance, their sebum contains

no squalene, hence they cannot be used for metabolic studies involving this substance. The use of genetically hairless strains of these animals enables samples of the surface skin fat to be collected at frequent intervals without the necessity of shaving the skin. Such studies are now in progress and will be reported fully in due course; it is hoped that these will prove of great value in the dietary control of seborrhœic conditions.

Clinical studies so far have been concerned with the seborrhœic conditions and with psoriasis; relatively few observations have been made on other conditions. Although these two conditions are likely to prove most fruitful for investigations of this type there is no reason to believe that changes in sebum composition do not play an etiological role in other skin diseases.

CONCLUSIONS

The study of the activity and metabolism of the sebaceous glands of man and other animals is still in its infancy, and so far has yielded little of clinical diagnostic value. Some use may be made of direct measurement of sebaceous activity in eliminating people with low sebaceous activity from occupations involving the use of defatting agents, thus reducing the incidence of sensitization reactions. Study of the chemistry of sebaceous secretion is helping to throw light on the etiology of certain clinical conditions of the skin. It is hoped that this line of research, if pursued, will lead to the development of better methods for the treatment of these conditions.

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PRESENTING SYMPTOMS AND SIGNS OF MALIGNANT DISEASE OF THE UPPER RESPIRATORY TRACT

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Any surgeon who has to treat cases of malignant disease of the upper respiratory tract knows very well that in all too many the disease is far advanced before specialist advice is sought. There is a number of reasons for this. The presenting symptoms are often slight and common ones and do not raise any alarm in the mind of the patient. It is difficult for the patient's practitioner to see well the various possible sites of disease. Inspection of the nasopharynx or the larynx and lower pharynx is often extremely difficult even for the expert and experienced laryngologist.

What must be emphasized is that any symptom which persists for more than two or three weeks, even if it is a common one like nasal obstruction or discharge or huskiness or slight discomfort in the throat, demands most careful examination to exclude malignant disease. If the practitioner is not satisfied that he can see well the region that appears to be affected and giving rise to symptoms, he should readily refer the case for expert examination. One must always be suspicious and on the alert to find malignant disease in its early stages, particularly in those patients over fifty years of age.

THE NOSE AND NASAL SINUSES

Unfortunately in most cases the early symptoms are the common ones of nasal discharge and obstruction. By the time many patients come for treatment the disease is no longer early and some swelling of the face or alveolus is obvious; or the swelling may have produced epiphora (table I).

Proptosis, slight or marked, or diplopia may send the patient to his doctor. There is at times a slight asymmetry of the mouth, with perhaps a little drooping of its corner on the affected side. The loosening in its socket of an apparently healthy tooth or sometimes pain in a tooth or the gum may raise suspicions: certainly when a socket fails to heal normally after dental extraction the question of malignant trouble should be kept in mind and x-ray examination of the adjoining sinus and perhaps biopsy or exploration be carried out.

The onset of polypi for the first time in one side of the nose in an older patient is always suggestive of the possibility of malignancy. So indeed is the unilateral development of chronic sinus infection in anyone of advanced years.

Pain is occasionally a striking symptom: numbness of the cheek or gums due to pressure on nerves must always raise suspicions.

One patient of over seventy years of age, happily alive and well five years after treatment for antral carcinoma, had been submitted to separate operations for the removal of polypi, drainage of the antrum and the frontal sinus before the occurrence of an alveolar swelling, which ulcerated, brought her for treatment.

Swelling of face or alveolus	12
Pain in face or gums	9
Nasal obstruction	7
Nasal discharge	5
Epistaxis	2
Epiphora	2
Headache	2
Numbness of gums	1
Not stated	1
Total	41

TABLE I.—Presenting symptoms and signs in 41 cases of malignant disease of the maxillary antrum.

Unilateral blood-stained nasal discharge demands careful investigation and certainly x-ray examination, when any thinning or erosion of bone may be taken in most cases to indicate malignant disease. Similarly, any unusual amount of bleeding on the removal of nasal polypi or a firmer or meatier appearance than normal in the polypi should lead to further investigation and microscopical examination.

THE NASOPHARYNX

The early symptoms are not alarming to the patient or to his doctor. Most commonly there is some nasal obstruction or discharge, either nasal or post-nasal, and this may be blood-stained (table II).

Nasal obstruction			32
Lump in neck			22
Deafness			19
Nasal catarrh			10
Pain	Throat	6	23
	Head	5	
	Jaw or face	5	
	Ear	3	
	Neck	3	
	Eye	1	
Epistaxis		5	8
Blood-stained discharge		2	
Blood-stained sputum		1	
Otorrhœa			3
Tinnitus			3
Blurred vision			2
Diplopia			2
Other symptoms or not stated			13
Total			137

TABLE II.—Presenting signs and symptoms in 137 cases of neoplasm of the nasopharynx.

A patient of over sixty, who came for treatment of his nasopharyngeal growth, had been submitted two months or so before to an operation for the straightening of a deflected septum to cure his nasal obstruction.

Deafness is a not uncommon presenting symptom. It may be relieved for a time by Eustachian catheterization and its cause may be overlooked. In one case in which secretory otitis media developed, the evacuation of the fluid by incision of the tympanic membrane postponed for a time the treatment of the causative neoplasm.

Pain referred to the jaw or face, or to the temple, or the ear or even the back of the head, is in some cases a prominent symptom—unfortunately not necessarily early. In too many cases the advent of cervical glandular enlargement indicating metastases is the cause of advice being sought. In a number of patients eye troubles—diplopia or blurring of the vision—call for examination. A squint due to external rectus palsy from involvement of the sixth nerve may be what brings the patient for consultation.

In one patient who had repeated epistaxes the nasopharyngeal neoplasm was overlooked until the nerve supply of the palate, pharynx and larynx was affected with consequent palsies producing symptoms.

GLOSSO-EPIGLOTTIC AND VALLECULAR REGIONS

Here there may be soreness in the throat, particularly on swallowing food or, less commonly, saliva. In some cases food seems to stick in the throat or there may be real dysphagia. In others an enlarged cervical gland will first draw attention to serious disease. The feeling of a lump in the throat always demands careful examination and in the vast majority of cases no organic disease is found, but this may be an early symptom of malignant trouble. So may be the slight feeling of discomfort or irritation, or the patient's idea that a foreign body is present in the throat. Blood-staining of the sputum and pain on swallowing referred to the ear are also suggestive symptoms.

Lump in neck	30
Sore throat	28
Dry throat or discomfort	7
Lump in throat	7
Dysphagia	5
Pain in neck	2
Pain in ear	1
Cough	2
Voice change	2
Bleeding	1
Other symptoms	5
Not stated	4
Total	94

TABLE III.—Presenting signs and symptoms in 94 cases of malignant disease of the tonsils.

One of the difficulties of diagnosis is that this region cannot be seen by means of the ordinary examination of the throat with a spatula. The laryngeal mirror must be used. Even with this, complete inspection may not be easy in some patients, and a long and forward-curved epiglottis will hide much of the vallecular region. A good habit to acquire is the ready use of the finger to palpate any accessible region in the throat, the base of the tongue, the vallecular regions and epiglottis and the tonsillar and faucial areas; any hardness or firmness may excite suspicion and indicate biopsy.

Sore throat	43
Hoarseness	26
Lump in neck	21
Dysphagia	20
Pain in throat	10
Discomfort in throat	9
Pain in ear	2
Cough	1
Other symptoms	6
Total	138

TABLE IV.—Presenting symptoms and signs in 138 cases of malignant disease of the pyriform fossa.

THE TONSILS AND THE PYRIFORM FOSSA

The tonsils.—Here the presenting symptoms are very similar to those just recorded for the glosso-epiglottic and vallecular regions, as table III shows. One must be ready to palpate the tonsil region and any suspicious area demands biopsy. The primary lesion may be very small and little more may be seen in the affected tonsil than slight enlargement or slight prominence.

The pyriform fossa.—Here again the early symptoms are slight and so often met with by the patient or his medical adviser that at first they may be disregarded and valuable time lost in palliative remedies before more radical treatment is instituted. There is usually soreness or pain on swallow-

ing food. But sometimes there is soreness or slight discomfort only and it may be felt on swallowing saliva and, at first, not with food (table IV).

In a patient seen last year this was the case and pain on swallowing food did not develop until a biopsy had been done.

THE LARYNX

The only early symptom in malignant laryngeal disease if the *glottic* region, that is, the vocal cord, is involved, is huskiness or hoarseness. There is no other early symptom at all. Only too often when a patient presents for examination and treatment one finds that the change of voice has been present for many months or even a year or more. The symptom is a common one, not at all unusual and not in the least alarming. Colds are so common that many, many times it is thought that the symptom is the aftermath of a cold. Only too often inhalations and lozenges are prescribed with consequent delay in establishing the correct diagnosis. In most cases the patient's doctor will be unable to examine the larynx properly and thoroughly. There is only one really safe course. Any huskiness or hoarseness which persists for three weeks in spite of simple treatment should be a strong indication for referring the patient for specialist examination.

With cases of cancer of the *supraglottic* region (e.g. false cords, ventricle) the presenting symptoms may be late in appearing and at first rather vague and slight. As a rule there is a change in voice and huskiness or hoarseness supervenes, but the symptoms may at first seem more indicative of pharyngeal disease: discomfort in the throat, soreness or pain on swallowing or dysphagia. Sometimes referred pain to the ear and, not so very uncommonly, enlargement of cervical lymph nodes may call for attention.

In *subglottic* cancer symptoms may be slight until the edge of the vocal cord is involved or its movement impaired, when huskiness or hoarseness is evident. Before this there may be a slight feeling of discomfort, the voice may tire easily or there may be intermittent huskiness. It will be only rarely that the growth will have enlarged so much that stridor or difficulty in breathing is present before advice is sought but occasionally this does happen.

SUMMARY

It will thus be seen that malignant disease of the upper respiratory tract causes no special symptoms indicating their serious nature, but rather the symptoms common to many much less serious affections. It is therefore essential that any symptom should be carefully regarded, that examination of the patient should be adequate and that in any case of doubt specialist examination should be advised. It is only by taking note of the earliest symptoms that cases of malignant disease will be found in their most treatable stage.

My thanks are due to my colleagues of the Royal Marsden Hospital for allowing me to give the figures quoted and particularly to the records department and to Mr. P. M. Payne of the cancer registry of the Hospital for his great help.

GENERAL PRACTITIONERS' FORUM

ACCLIMATIZATION DIFFICULTIES IN THE UPPER ENGADINE

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SHOULD older people, with hearts that are not quite intact, or with hypertension or arteriosclerosis, break the journey from the lowlands to the upper Engadine with a day of rest half-way up? I do not believe that such a break at an altitude of 3000 feet (920 metres) assists the acclimatization to 6000 feet (1,840 metres). The advice often given by the family doctor, to break the journey with a rest day half-way up, is based upon the mistaken belief that, with increasing altitude, the growing demand made upon the circulatory system can be represented by a straight line. Up to about 4000 feet (1,220 metres), it is rare to find any difficulty in adaptation, and it is only between 4000 and 6000 feet (1,220 and 1,840 metres) that such disturbances begin.

THE SUBNORMAL HEART

These disorders do not appear so suddenly as one would expect. A visitor with a slightly defective heart may stand the journey up without discomfort, spend the first night well and feel so fit on the following day that, stimulated by the marvellous alpine air, he will take a long walk in the afternoon, eat well and go early to bed, well satisfied with his day's performance. Shortly after midnight, however, he may wake up with a need for air which forces him to spend the long hours to morning sitting up in bed or at the open window. He sends for the doctor, who will note that the degree of demoralization of the patient is in marked contrast to the lack of clinical symptoms. Sighing gently, he will see, not for the first and certainly not for the last time, that the circulation tests which are at present *de rigueur* can only supply him with the vaguest of notions of what kind of heart the patient has, what it can achieve and what is its fate.

Healthy individuals of any age achieve acclimatization so easily that the processes involved occur below the threshold of consciousness. But, if someone who lives in the lowlands becomes ill in the Engadine, even if it is only a simple chill or indigestion, this slight upset of the biological equilibrium may undo the whole process of adaptation and produce manifest disorders of acclimatization which are equally unpleasant for patient and physician and may prolong the period of convalescence. In February, for instance, the influenza, which is imported from the towns of the lowlands, can become epidemic. If it attacks older visitors, it subjects them to a serious strain at this altitude.

It is a popular, but often mistaken, belief that the 'pure mountain air' will effect a welcome aid to convalescence. For all patients, except those

who are only slightly ill, I advise a return to the lowlands as soon as they are able to travel, since there they will recover much better and more rapidly. Nevertheless, it is a paradox, but a frequently observed fact, that a journey to the Alps during the convalescence of a patient living in the lowlands can be very advantageous, so long as the illness has not seriously damaged the heart.

CORONARY DISEASE

In what circumstances should the practitioner forbid a holiday in the Upper Engadine? There is only one absolute contraindication: angina pectoris, be it ever so slight. The doctor who does not expressly warn such a patient against the Engadine takes upon himself a grave responsibility.

An Englishman of about 55, an enthusiastic and experienced alpinist, had spent every summer in the Alps and had climbed the highest peaks without suffering any adverse symptoms. Then, one winter, he had a myocardial infarction. He recovered remarkably well and, despite the warnings of his physician, decided to come to the Engadine the following summer. He felt so well on arrival in Pontresina, that he set off on the second day with a guide on a climbing tour which was not particularly difficult but which meant a long and tiring march. The damaged heart did the work its master gave it, but no sooner had he finished the tour than it stopped beating.

I can recall several similar, if less dramatic, cases. It is strange that in all of them death occurred during, or immediately after, the homeward trip, which confirms the old experience that even a badly damaged heart still shows an astonishing reserve of strength at its command.

In middle-aged visitors whose hearts have hitherto met all the demands of everyday life without apparent effort, cardiac pain may appear for the first time at high altitude, ranging from slight warning signals which the patient often does not gauge correctly, to severe myocardial infarction.

A Bernese lawyer in his fifties had to change the wheel of his Chrysler single-handed on his arrival at St. Moritz. During the night he woke up with all the symptoms of a fresh infarct.

A well-known English specialist of the same age had spent his winter holidays in the Upper Engadine for years. Suffering from the puritan inability of the Anglo-Saxon to practise a healthy 'dolce far niente', he hurried off as soon as he arrived to the practice slopes for the ambitious skier. (This sport, incidentally, has ceased to be a harmless amusement and is practised nowadays with a dour seriousness. The slopes, or 'pista', are worn so smooth, and often so iced, as to make a comfortable pace impossible; they demand a fierce tension of all the forces of body and spirit. Serious accidents are frequent; fatal ones, due to collisions or falls at high speed, are by no means a rarity.) On the second day after his arrival, he was stricken by a myocardial infarction while skiing. Luckily, after this dramatic start, the condition evolved favourably, but the contented faith in his own health which this busy man needed in his work, was lost in the Engadine, and he will hardly risk coming up again.

ASTHMA

Bronchial asthma has long been considered an indisputable indication for an alpine cure in the Upper Engadine; unfortunately this is but another example of the age of a dogma being no guarantee of its reliability. When children up to 14 years of age spend one to two years without a break in the Upper Engadine, a permanent cure can be expected in only half the cases at the most. Such a long-term cure requires considerable sacrifice,

even from well-to-do families, and little consideration ever seems to be given as to whether it is really worth while taking a child at the most important phase of his development out of the milieu into which he was born, and breaking the chain of his schooling to bring him into strange surroundings and to sow the seed of a belief that he is an ill child and therefore justified in making demands upon society for special sympathy and consideration.

The family doctor will do well to exercise some restraint in recommending an alpine cure for asthmatic children, and all the more so in the case of adults. Not infrequently it happens that adults with a long and trying asthma history are sent up to the Engadine and given hopes that a few months at high altitude will be sufficient to effect, if not a final cure, then at least a long-lasting improvement. These patients have grown up with their asthma; for years the asthma has been attacked by the arrows (sometimes slightly poisonous) of modern anti-allergic therapy. And now, suddenly, a few months of breathing in the mountain air is expected to bring about a happy ending to the faulty biological reactions which the patient has had for tens of years! At the best, when the high altitude is well tolerated, the attacks are less frequent and there may be a temporary improvement: a poor result when judged in relation to the expenditure of time, money and faith. Not uncommonly the lack of allergens in the mountain air is more than offset by the burden of the altitude upon the right heart which is always damaged in older asthmatics. In such cases, after a few days, the rapid and threatening increase in decompensation puts an end to the high-altitude cure which was started with such high hopes, and the patient returns home worse off than before.

It is a different matter with asthmatic subjects who take their affliction in their stride, so to speak, and after a bad night carry on with their daily work: in other words, those individuals who do not allow themselves to become the slaves of their affliction. In the Engadine they can enjoy the freedom from attacks for a few weeks without harbouring any illusions about a permanent cure. A curious fact may be mentioned here: the first fall of snow at the beginning of winter produces a severe attack in many asthmatics, even when they have been without an attack for months. No-one knows why.

CONVALESCENCE

People who are severely exhausted, whether owing to illness, overwork, worry or anxiety, may seek in vain the recovery they long for in the Upper Engadine; all too often their condition deteriorates at high altitude. Why is this? The banal and highly unscientific explanation would be that the lowlander who hopes to make use of this aggressive climate, with its intense sunshine, its brusque changes of temperature and its constant cool winds, must have a certain reserve of energy to stand a climate which puts the human organism on the defensive, if he is not to become more exhausted by the constant effort of adaptation. It has long been known that hypochromic anæmia improves at high altitude, but there are exceptions to this

rule. If there is serious exhaustion as well as anæmia, then a journey to high altitudes may produce a further decrease in hæmoglobin.

The director of the meteorological station on the Säntis (7,500 feet [2,280 metres]) once developed a severe anæmia as the result of an accident. Blood groups were not yet discovered and a blood transfusion was impossible. The doctors expected that the high altitude would accelerate the regeneration of blood, but they were wrong. It was only after the patient went down to the lowlands that recovery began.

In schoolchildren and young women of the Upper Engadine hypochromic anæmia is no rarity; the paradoxical but efficient therapy is a few weeks' holiday in the lowlands. It is also a paradox, but a fact which is often confirmed, and too little considered today, that patients with hyperthyroidism, even the severe cases, often benefit from a few months' stay at high altitude, with a favourable effect upon the metabolic rate. It is also curious that many hypertensive persons of advanced age return again and again to holiday in the Engadine, because they maintain that they can breathe better, sleep better, eat better and walk better than they can at home.

The fear of many hypotonic patients (or rather the fear of their doctors) of venturing into high altitudes is unjustified. Actually they can acclimatize without any difficulty so long as they keep quiet for the first two days. After that, they can undertake even long walking tours so long as they go slow at first and keep to a snail's pace until 'the engine is warmed up'. Once they have their second wind, they can keep up with the best without overtiring themselves.

TREATMENT

And now a few words on what contribution therapy can make towards alleviating disturbances in acclimatization. It is not advisable, and indeed it is usually a waste of breath, to try to persuade the visitor to stay when any of these dramatic disturbances occur soon after his arrival in the Engadine; it is wiser to help him to pack his bag and leave. The attempt to give drugs for disorders of acclimatization is only justified when it is needed to balance what the bankers call an 'emergency credit': i.e. to support the organism through the difficult transition until it is able to help itself again.

There are certain harmless, but annoying, disorders which not infrequently occur at medium or high altitudes during the first days, even in healthy individuals, especially in cigarette smokers: for instance, some degree of breathlessness at the slightest effort, uneasy sleep with anxiety dreams, and a fluctuating depressive effect which prevents the realization of the anticipated holiday mood. These symptoms usually disappear rapidly if a mild sedative is given. The new 'tranquillizers' are best left alone; the small dose of peace of mind which they produce is precarious and too dearly bought. It is sufficient to prescribe such harmless drugs as phenobarbitone in small doses, combined, if necessary, with a drug acting on the peripheral circulation: e.g. 'sympatol'.

ANGINA PECTORIS

At the first appearance of any symptom of myocardial pain, even in a mild

form, immediate return to the lowlands must be ordered. But what is to be done in the case of a fresh infarct? The patient is between the devil and the deep blue sea. The high altitude puts a severe strain upon the damaged heart, and this strain should be removed as soon as possible; but a fresh infarct calls for strict rest in bed. Which of the patriarchs of cardiology laid down the dogma that the period of bed rest must last for six weeks? If the patient is a man in his best years, and the infarct tears him from his work to a sick-bed and faces him with the prospect of cutting down his whole mode of life to half-speed, may it not be supposed that the revolt of his entire personality may do the damaged heart more harm than would a few steps from his bed to an armchair at the window of the living room in the third week? All too often the atmosphere of the sick-room suffocates the will to live. The bosom of the supine man is more vulnerable to the attacks of depression and despair than is that of the man standing upright. The layman wonders whether the most important reason for those strictly prescribed six weeks may not be to provide the conscience of the *doctor* with this period of peace! In medicine, to allow requires more courage than to forbid.

On several occasions I have taken patients immediately after recovery from the first shock, that is on the third or fourth day, by ambulance to the nearest hospital in the lowland. This necessitates crossing the Julier Pass, the crest of which is 7000 feet (2,130 metres) high. The first time I did this, it was no light decision. Had the patient died of a fresh attack on the way, I should have been held responsible, and the journey over the high pass would have been considered a criminally irresponsible act which had cost the patient his life. The risk, however, was justified, and these patients showed on reaching an altitude of about 4000 feet (1,220 metres) a recession of the retrosternal pressure, greater ease in breathing and a remarkable improvement in general condition. Much greater altitudes than that of the Julier Pass are tolerated by those with heart disease so long as they are there for only a few hours.

ADVICE FOR VISITORS

Finally, a few words of advice for future holiday visitors. To overtire oneself is a bad start which may easily ruin the whole holiday. For the first few days, no big tours should be made. Taken in small doses, the sunshine of the Engadine can be a tonic, but it is not a commodity to be taken *ad libitum*. Intensive sunbathing may lead to burns of the first and second degree, and it can also lead, when combined with strenuous physical effort of an untrained body, to much worse damage, as the following case, which is rare but instructive, will illustrate.

A blonde and somewhat puffy girl of 22, who had been working in the laboratory of the Samaden hospital for several months, and who was acclimatized but not in physical training, joined a Sunday ski tour in March—hatless and in brilliant sunshine. The climb was not difficult but entailed an ascent of about 2000 feet (610 metres). This the girl could have managed easily, even without training, if she had taken her own pace to suit her strength, but the pride of sports would not let her

lag behind the others, and she forced more effort out of her body than it could manage without damage, and arrived at the top in a very exhausted state. On the descent, which is not easy even for a good skier, she fell often and arrived overheated but apparently healthy and in good cheer, and even arranged an informal gramophone dance for her companions. After half-an-hour, however, she was seized with a violent headache and had to lie down. Half-an-hour later she was unconscious, and in the early hours of the morning she died in deep coma. The necropsy revealed numerous fresh miliary hæmorrhages throughout the whole cerebrum.

CONCLUSION

For the visitor to the Upper Engadine, one of the most fascinating landscapes on this planet, there is a wise old French proverb: 'Il ne faut pas abuser les bonnes choses du bon Dieu'.

DOCTOR IN SEARCH OF A JOB

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Edinburgh

I am looking for a job. So, I gather, are many of my colleagues, and while I cannot recommend this pursuit to others (popular though it may seem), it is not without its rewarding moments, and certainly helps to shed some light on that august and esoteric body, the British Medical Profession.

THE SEARCH

The highlight of my week is Saturday, the day on which the *B.M.J.* is delivered. To extract it from its paper cocoon is but the work of a second. The pleasurable feeling of anticipation is equal only to that provoked by the Saturday evening sports final with its promise of confirming the 'Four Aways'. Is there anything in it for me? I skip the articles on the latest subdivision of the Rhesus blood groups, try not to look at the letters foretelling the downfall of all doctors under the N.H.S., and arrive at the advertisements. By this time, my wife has joined me, and the game begins. Would we *really* like an island in the Hebrides with 154 patients? Dare one apply for a vacancy (private patients only) at Budleigh Salterton? At any rate I write for copies of what must be the oddest form on which anyone has ever had to apply for a post—the E.C.16A.

The 'Assistantships Vacant' column provides the bulk of the morning's work. Why are doctors so secretive? To have a box number is fair enough, but merely to hint vaguely as to the whereabouts of the practice concerned suggests a hitherto unrecognized shyness in doctors. The habit, however, does provide the basis of a fascinating type of Panel Game (B.B.C. please note). 'East of Scotland University Town' was easy. 'Southern Seaport Town' opened up a wider range of possibilities. 'Northern Industrial Suburb' I felt was really unfair.

Any advertisement mentioning a 'view' can expect twice as many applicants as other advertisements, and this well-known carrot is dangled in

various ways, and with varying probabilities of its being fulfilled. A view, after all, merely suggests a possibility of partnership. So what is a 'possible view'? The author of 'Possible view to suitable applicant after period of trial' displays a genius for vague circumlocution and a desperate fear of committing himself.

Before drawing up my list of what I hope are 'This Week's Winners', a glance at the back pages of the Journal is instructive and often a boost to the imagination: 'Medical Officer at a British Embassy with a tax-free allowance of £2000'; 'Medical Officer to the J. Arthur Rank Film Company' (My wife says 'Try it'); 'Doctor for an Antarctic Expedition' (My wife says 'Don't'). A list is finally made, however, and the job of writing applications begins.

THE APPLICATION

I have always submitted what I think is a legible explanatory letter, enclosing fresh copies of at least four testimonials. At first, I confidently expected an acknowledgement of each letter. I find, however, that at least 50 per cent. of my applications are never answered. A short trial period of enclosing stamped, addressed envelopes produced no better results. I now count myself lucky if after two or three weeks my testimonials are returned, crushed into an envelope too small for them, with the fifth carbon copy of a note starting 'Dear Doctor'. (Since I discovered that paper can be ironed, my typing overheads have been reduced, while prospective employers continue to get fresh copies of testimonials.) I post my applications, and wait.

THE INTERVIEW

Occasionally an advertiser rises to the bait, and an interview is suggested. This is the prelude to an interesting insight to a wide variety of practices. I have been made to feel like an office boy seeking a position as head clerk. I have had to sit in the waiting room while the previous candidate was being examined, only to hear, half way through a rushed type of grilling, the next candidate arriving. I have been to interviews where I had to ask all the questions to avoid sitting in stony silence, and interviews where my main purpose seemed to be to listen appreciatively to glowing accounts of the practice concerned. All types are met: from downright rogues to benevolent gentlemen of the old school.

CONCLUSION

The doctor seeking an assistant today is very much in a buyer's market, and unfortunately one meets those who take advantage of this position. But just as one is losing faith in the profession, something happens to restore it: a courteous reply to a letter; an interview at which kindness and hospitality are offered. And so the search for one's ideal practice goes on.

The lot of young doctors seeking entry into general practice today is not a particularly happy one. The position might be eased if certain points were observed. Advertisers should state exactly what is offered and exactly what is required. The precise locality should be stated. A letter merits a reply.

SECTION OF GENERAL PRACTICE OF THE
ROYAL SOCIETY OF MEDICINE

DISCUSSION ON HYPNOTISM IN GENERAL PRACTICE

March 19, 1958

Dr. H. Stewart (*Watford*).—So far the use of hypnotism has been as a therapy to fall back on when more orthodox treatments have failed. In general practice it will therefore be used on the 'chronics' whom no-one has been able to help. Of those to be treated, 90 per cent. will be hypnotizable but only 20 per cent. will go into a deep somnambulistic trance. Fortunately this deep trance is not essential for most hypnotherapy but the fact remains that the deeper the trance the greater is the range of hypnotic techniques that can be used.

TECHNIQUES

The techniques, to be used when the patient is in the trance are:—

(i) *Simple suggestion.*—All doctors use this when treating patients but when used in a trance it is a much more powerful weapon and can be used for symptom removal. Herein lies its danger since the symptom can be removed and the underlying pathological state, either organic or psychic, has not been eradicated and will tend to give false 'cures'.

(ii) *Educative.*—This consists of teaching a patient symptom-removal by autohypnosis, and is really one aspect of post-hypnotic suggestion: e.g., autorelaxation in asthma.

(iii) *Removal of inhibitions.*—Patients talk of their emotional problems more readily in a trance and, in addition, the words are often charged with emotional effect.

(iv) *Obtaining of emotional abreactions.*—This is an extension of (iii) and occurs when some past emotionally-repressed terrifying experience is relived during the trance: e.g. of shellshock or a bad railway accident.

(v) *Age repressions and hypnoanalysis.*—For all practical purposes this can only be shown in deep-trance patients. The patient is taken back to earlier years of his life, relives them and produces hidden memories from that period. It is thus a valuable analytic tool in hypnoanalysis: an investigation into the dynamics of the patient's psyche while in the hypnotic trance. Unless the practitioner has extensive knowledge of psychodynamics, it should not be attempted.

THE MAIN USES OF HYPNOSIS

(i) *Psychosomatic disorders.*—In this group are included the patients with asthma, eczema and urticaria, gastro-intestinal disorders, migraine, and the like. The ideal of treatment is symptom removal and settling the associated emotional conflict, but strangely enough the latter is not always necessary and symptom removal in itself is sometimes sufficient.

(ii) *Psychoneurotic disorders.*—In this group anxiety states and conversion hysterias can be tackled. In a trance inhibitions are removed and the patient is encouraged to speak. If the situation merits it, emotional abreactions are obtained. The material is worked through with the patient and he is enabled to see his conflicts in as clear a light as possible. Many sessions may be spent on this form of psychotherapy.

(iii) *Organic disorders with tension-anxiety overlay.*—In an organic disorder, the symptoms may be more disabling than can be accounted for by the organic lesions present. Here, symptom removal and investigation of the conflicts causing the tension-anxiety are often very helpful to the patient.

(iv) *Some other uses.*—In midwifery to obtain lack of fear, relaxation and, in a good subject, complete analgesia. In surgery to obtain lack of fear and again, if possible, anæsthesia. Its suggestive qualities are also of use in stopping excessive smoking and eating and also nail-biting.

The chief drawbacks of hypnosis are that it is time-consuming and that it may tempt the doctor to attempt too much on too little knowledge. Research is still very much needed to estimate its real value.

A. A. Mason (*West London Hospital*).—Before hypnosis can be accepted as a therapy today, it is necessary to examine why it has been abandoned so often in the past. The doctor and the patient have both played a part in its fluctuations: the patient by refusing to accept limitations in medicine, searching for magic and wanting hypnosis to fulfil this desire; the doctor by deluding the patient and sometimes himself into the belief that hypnosis is magical and will cure all incurable illness. Among people practising hypnosis there has been a high percentage of frank charlatans and inadequate failures who used hypnosis to give themselves a sense of power. The combination of magic-searching patients and unscientific or quack practitioners has resulted in the rise and fall in the popularity of hypnosis. The real, if small, number of genuine cures is lost in the muddle of claims and counter-claims.

Today there is another upswing in popularity which is being backed by a few controlled therapeutic series, but still a large number of exaggerated and uncontrolled claims throw doubt on the whole procedure.

THE SCOPE OF HYPNOTISM

Hypnosis can be practised by all, is simple to learn and requires no special ability or power. Specialists and special clinics only serve to suggest that there is something 'special' about hypnosis—which there is not. Some 80 to 90 per cent. of people can be hypnotized and all techniques produce a trance state by repeated rhythmical, monotonous sensory stimulation. It is similar to the sleep induced by the mother rocking her baby or the train lulling its passenger.

Analgesia can be suggested and occurs in various degrees in the trance state. Major surgery can be performed in a deep trance, which is an ideal anæsthetic, but can only be produced in 20 per cent. of patients. Fifty per

cent. of patients have sufficient analgesia for minor surgery such as dental fillings, reduction of fractures and dislocations in the casualty department, painful dressings and all repeated and multiple painful procedures in the sick, the young or the apprehensive. It is a valuable adjunct to local analgesia and as a premedication for general analgesia. It is an especially valuable analgesic for obstetrics, giving pain relief in a high proportion of cases without interfering with the mechanics of labour or depressing the infant's respiration. It has also been used in the intractable pain of trigeminal neuralgia, causalgia and inoperable carcinoma. Hypnotism is especially useful for the removal of the psychological overlay of pain, whether the pain be caused by surgery, chronic disease or parturition.

Direct hypnotic suggestion aimed at symptom removal is often useful in psychosomatic disorders such as chronic skin diseases. A 50 per cent. recovery rate over four years has been recorded in 200 previously chronic cases. Asthma is being treated extensively and a percentage of cases undoubtedly respond favourably when other treatments have failed. Patchy results have been obtained in colitis but investigation into this and other gastro-intestinal disorders is proceeding. Some sexual difficulties have responded but the results are not impressive. Warts, which respond to all forms of suggestion, do especially well under hypnosis, and all multiple and resistant cases should be considered suitable.

Habits and mild addictions, such as nail-biting, cigarette smoking, overeating and hiccups, respond favourably; the more severe addictions usually require psychotherapeutic intervention. It is probable that psychosomatic disorders are in fact psychoneurotic disorders which are converted into 'body lesions' by the patient for various unconscious motives. Hypnotism sometimes reverses the process and changes the conflict into a more therapeutically accessible form. Psychotic conversion does not occur in a greater incidence than would be expected to occur normally. Hypnosis is being used more often in psychiatry to help in speeding up certain forms of psychotherapy. Its uses range from simple symptom attack to complicated analytical processes in the hypnotic state: these, however, are specialist fields.

Undoubtedly hypnosis is of more use to the general practitioner than to anyone except perhaps the anæsthetist, and he should certainly have a working knowledge of its uses and limitations. Only in this way will desperate patients be prevented from seeking treatment from lay practitioners.

C. A. H. Watts (*Ibstock*).—My introduction to hypnotism was perhaps a little unfortunate. The subject interested me and when, in the army, I was sent on a course to a psychiatric centre, I thought that I might see some of this treatment. When I asked the psychiatrists to demonstrate it to me, like the wedding guests of the Bible, 'all with one consent began to make excuse'. So I had to teach myself the art. I used hypnotism occasionally over a number of years, but in the end I gave it up. In this paper I outline the reasons why, for me, it has lost its appeal.

THE DISADVANTAGES OF HYPNOTISM

According to the literature a wide range of illnesses can be benefited by hypnotism. Asthma and enuresis can be cured: habits such as smoking can be dropped, not to mention a whole host of psychological disorders. Many of the conditions named are intractable and very troublesome to both consultant and general practitioner. If hypnotism is so safe and so effective, why has it not been widely used by the profession as a whole?

To practise the art successfully one must have the right type of patient. It was because hypnosis did not work in some of his patients that Freud gave it up as a routine practice. Strauss suggests that, whereas 90 per cent. of people are susceptible to light hypnosis, only 40 per cent. pass to a deep level, and only 10 to 15 per cent. can be sent into the type of coma in which surgical operations can be performed. In my experience the patient who will agree to this type of treatment is the exception and not the rule. This uncertainty is a disadvantage, and the mystery of its mode of action puts some of us off. A fellow-practitioner told me how by hypnosis he had completely removed the pain of herpes zoster from a patient. It is difficult to understand how an organic pain of this nature can be allayed. It is magic! One could argue that, although we do not know just how E.C.T. works, many of us make good use of it. The difference is that if we apply the current we can be quite sure that the patient will have a fit. As in hypnotism, the outcome of the treatment is not so certain, and it is because of the failure rate that these methods of treatment are to be avoided in general practice. Failure to help the patient with major treatment of this kind can be compared to the embarrassment of failed forceps in obstetrics.

Even more important than the right type of patient is the right type of doctor. Only a very small proportion of doctors can stare confidently into their patients' eyes using the formulæ of the hypnotist. The family doctor who practises hypnotism is apt to become labelled and this is undesirable as some people are fearful of the procedure and the doctor who uses it.

Frank hysteria is the ideal case for hypnosis, but it is a great rarity in general practice. There are usually easier alternative methods of treatment. Advocates of hypnosis argue that they can get at the root of the trouble more quickly, but hypnotism is a time-consuming treatment. Stewart suggests that he spends four to eight hours on his cases, and this is no quick cure.

For most of us there is plenty of psychiatry in general practice without filching hypnotism, narcoanalysis, E.C.T. or even the couch from the psychiatrist. I would suggest that, if a doctor cannot help his patients by a form of psychotherapy which can be performed with his patient sitting on a chair in the consulting room in the same way as any other patient, then the case should be passed on to a psychiatrist. I am all in favour of the general practitioner taking his full share of the psychiatric load, but it is a wise man who knows his own limitations.

PERSONAL IMPRESSIONS OF AMERICAN MEDICINE—I

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Nobody really suggested postgraduate study in America. It seemed a good idea when I was in the Navy and considering what to do on discharge. I had read about the Mayo Clinic and I had heard about the Johns Hopkins Hospital and its achievements during my medical school course. I chose the latter. I didn't really know of any other medical centres in the United States. My first application was replied to by a form letter. It was polite but explained that post-war crowding made more than a brief visit inadvisable. A few years later another request asking about a position as a house physician received courteous acknowledgement and a detailed application form in reply. This was sent off with the names of three referees. Almost a year later, when I had forgotten about it, a letter arrived, saying that my training suggested that I might be interested in experimental virus work. A pleasant exchange of letters followed and a final agreement was reached whereby I was appointed 'Fellow in Medicine (Full-time)' for a year as from July 1, 1949, at 'no salary'.

THE PRELIMINARIES

The absence of salary gave me something to keep me busy. When I graduated in a class of 170 I was probably in the upper third, but I obtained no particular distinctions and at this time I had no published experimental work. For this reason, because it was the wrong time of year to apply or because of a certain official caution that I was throwing my bread upon the waters, I was unsuccessful in some 10 to 15 applications for Fellowships. I was, however, successful in obtaining a travel grant from the U.S. Educational Commission in the United Kingdom under the Fulbright Scheme.

Under the terms of public Law 584 of the 79th Congress of the United States of America, known as the Fulbright Act, and the Joint Anglo-American Agreement of September 22, 1948, establishing the United States Educational Commission in the United Kingdom, travel grants are awarded to citizens of the United Kingdom who are going to America for an academic or educational purpose, such as study, research, instruction or pursuance of other education activities at, or in connexion with, an American institution of higher learning. It is a pleasure to record that Senator Fulbright who sponsored this law is a former Rhodes' Scholar.

This was a generous grant for cabin class travel. As I had by this time married a Canadian physician we were both able to travel on the grant in tourist accommodation which is quite luxurious.

We were advised to get an immigration visa in place of a student's visa so that my wife could work. This had one disadvantage that it made me liable to draft as a doctor into the U.S. Forces but my service in the Navy as a

doctor in wartime, at least to the present time, has been considered equivalent service. We borrowed £500 (at that time equivalent to $2000) which we took out of the country with the permission, if not with the blessing, of the Bank of England.

Our arrival on June 28, 1949, was not unheralded. As the first Fulbright grantee to arrive from Britain we were met by an official from the State Department who, in his own words, 'was there to see that our first impressions of America were good ones'. There were also three reporters and two photographers. Suddenly we were ashore. The State Department man had a card which was very effective in having our papers checked in extra quick time. A car and a hotel room were waiting. We declined the latter and moved into cheaper quarters at $3 daily. Our first impressions *were* good ones.

BALTIMORE

The main impression of our first few months was one of tremendous hospitality and friendliness. We were invited to many homes and there was always someone ready to take us there by car. We soon located a one-bedroom furnished flat almost across the street from the hospital, at $60 monthly. The rent included electricity and gas and the use of a gas cooker and an electric refrigerator. The latter is essential. In our poor days we found we could just live on $2000 yearly, but this would not be true now and $3000 to $3,500 might be the minimum. Thanks to the efforts of my chief, Dr. Mirick, we were able to relax financially when I was granted a U.S. Public Health Service Fellowship at $3,600 tax-free. As was true for the Fulbright grant, the application system was straightforward and all my dealings with the Fellowship authorities were very pleasant.

We began to learn a lot about Americans from our daily work, from the radio (on which you can hear *anything* including 'holy rollers' and symphony concerts), from *The Readers Digest*, from *Time* Magazine and from a very useful one-dollar almanack, 'The World Almanac', published annually by the *New York World-Telegram and the Sun*. Names are most misleading as Mr. Pulaski may be much more American than Mr. Smith. Americans are very straightforward and very democratic. Sometimes their democracy causes misunderstanding in that they have an unexpressed idea that the other fellow is free to do anything his way if he wants. If it is illegal the police should get after him but why should the ordinary citizen interfere. This principle, of course, applies only in minor infringements and otherwise people are quite law abiding.

In general there are very few false pretences in America. I like the story of the two men entering a restaurant: one was British and he walked in as if he owned the place, the other was American and he walked in as if he didn't give a damn who owned the place. One can always find faults (e.g., radio, bread, and some aspects of the postal service), but the over-all impression is one of wonderment that so many nationalities could have blended so quickly and with so many obviously excellent results.

THE JOHNS HOPKINS

The general atmosphere of the Johns Hopkins Hospital is one of its outstanding points. It is intangible: and somehow combines friendliness and an eager desire to know with a very pleasant intellectual leaven. As this school has contributed more teachers of medicine than any other in the country it has friendly connexions with all others. This does not mean that it receives no criticism. It receives plenty of the latter but is still undeniably a leader among the American medical schools.

Dr. Mirick was in charge of the biological division (infectious diseases division) of the department of medicine. The department is in several divisions each under the direction of an associate professor (usually a physician of 10 to 15 years' experience). Such departments often have a grant for basic expenses from the University but usually a large part of the money comes in various grants from independent or Government foundations. In some cases consultation fees received by full-time staff members go into the research fund. To obtain grants the senior investigator has to be a person of standing in research and has to submit a synopsis of his proposed research. As many of these grants are made on a year-to-year basis, a certain amount of insecurity is inevitable. Over a two-year period Dr. Mirick and I studied pneumonia virus of mice infection in relation to urethane, bacteria, ACTH and cortisone and its possible relationship to pulmonary adenomas in mice.

In some cases Fellows were encouraged to have two projects, one a necessary, though often lack-lustre, project which would always produce results of use to science and another more fundamental and more adventurous in spirit which might be a complete failure. A project of the former type was undertaken by Dr. Jordan and myself when we studied the diagnosis and treatment of liver tumours from the cases seen at the hospital.

Of the latter type of experiment, Dr. Mirick used to tell a story about a lady scientist who told her chief she was going to organize an expedition to the Himalayas to find Dinosaur's eggs. 'You don't expect to find any, do you?' 'Well no, but I might'. 'If you do, what will you do with them?'. 'I'll incubate them'. 'Well they certainly won't hatch'. 'No', she replied, 'but just *think* if they did!'

From time to time we did 'dinosaur egg' experiments which if they did nothing else were good for the morale. Also from time to time we would have free-thinking discussions when we spoke freely about developments without too much thought for the scientific backing for our statements, and usually with our feet on the table and a 'coke' in our hands.

In the ward for infectious diseases (a term interpreted liberally to include such things as subacute bacterial endocarditis), we saw such rarities as leprosy and some of the fungus diseases like blastomycosis of which we sometimes doubt the existence when reading about them in Britain.

Each Fellow was expected to spend at least one half-day weekly in medical outpatients clinic. This we did and I also spent a half-day in the liver clinic with Dr. Ratnoff. Americans are enthusiastic seekers after knowledge and nothing impressed us so much as the overflow attendance at a course for medical students arranged for Saturday afternoons!

THE 'AMERICAN BLACKPOOL'

In April or May, medical investigators from all parts of the States gather in Atlantic City, New Jersey, to give and to hear papers on diverse research problems. This 'American Blackpool' lends itself to such a meeting. It has large hotels and large meeting halls able to accommodate the 2000 to 3000 doctors who attend. Not all of these doctors are in research as many progressively minded physicians in practice also attend. The meetings are held by the Blood Club, The American Federation for Clinical Research (as this was founded by Dr. Christian it is sometimes referred to as the Young Men's Christian Association), The American Society for Clinical Investigation ('The Young Turks') and the American Association of Physicians. Certain seats are reserved for members of these societies but one does not have to be a member to attend. A great number of reunions take place here and a certain amount of job-hunting and placement also. Practically no advertising of posts occurs in America for academic positions in medicine: all the posts are filled on a letter, telephone and interview basis. The posts as interns, however, are filled by ballot. Senior medical students apply to the hospitals of their choice. These they list in order of preference and the hospitals in turn list the candidates of their choice. All lists are tabulated on I.B.M. machines. Under the auspices of the American Medical Association the choices are matched and offers of positions are sent out to newly graduated doctors. Eighty per cent. or more of the medical students receive their first choice.

ST. LOUIS

While with Dr. Mirick I decided to stay in the field of infectious disease. This required more clinical work and he suggested an assistant residency in internal medicine (equivalent to a resident registrarship). To this end I applied to a list of hospitals in the United States and Canada (16 in all), which we prepared jointly. I was delighted to hear in the September preceding the appointment in July 1951 that I had been appointed an assistant resident on the ward service of Dr. W. Barry Wood, Jr., at Barnes Hospital and Washington University, St. Louis, Missouri.

I began to appreciate the tremendous size of America on my 800 mile trip from Baltimore to St. Louis. We transported our worldly goods by railway freight for $75 but had been quoted a figure nearer $400 to do it by moving van. The city of St. Louis has a population of approximately a million and is on the west bank of the Mississippi some miles below the mouth of the Missouri. The state of Missouri is almost as big as Great Britain but has only four million inhabitants.

There are two medical schools in St. Louis: at Washington University and St. Louis University. The name Washington University is a little confusing as there is also a State University of Washington in Seattle, Washington, and a George Washington University in Washington, D.C. In Washington University there were three professors of medicine.

POSTGRADUATE TRAINING

In the United States, organization of postgraduate training in internal medicine follows fairly standard lines. The graded training as an intern then as an assistant resident and further as a resident in medicine is something peculiar to this Continent. Parts of the training have been used elsewhere but the combined grouping is unique. The newly graduated M.D. begins his work in a hospital as an intern looking after usually from 10 to 20 patients. This may be a rotating internship (including medicine, surgery, obstetrics, etc.) or a 'straight' internship (only medicine, only surgery, etc.). The period of training lasts one year and is in many cases subdivided into work in the main teaching hospital, work in another subsidiary hospital, experience in the laboratory and experience with neurological or other patients with diseases of a specialized type. The intern works under the direct supervision of an assistant resident, the post of assistant resident being filled by a graduate one or more years out of medical school. The assistant resident may be responsible for the organization of part of the teaching of three to eight medical students. The assistant resident rotates through the various services such as female and male medical wards, neurological and metabolic wards (recently reintegrated with general medicine in St. Louis) and the clinic. The training at Barnes Hospital until recently included a free period of two months when the assistant resident joined with a member of an experimental team or did work on his own in a chosen field or read in the library if he wished.

THE CLINIC

In the clinic about 600 patients were seen daily, approximately 90 of whom were seen in the internal medicine clinic. The staff of the department of internal medicine is also responsible for the screening clinic which is the key to the whole system of specialty clinics. Every patient arriving at the clinic is seen by an assistant resident who in a short interview, usually about two minutes, decides where this patient should be sent for investigation. There are four assistant residents working in the medical clinic and they take this job as screening doctor in rotation. During a typical week, 135, 107, 104, 83, 64 and 28 patients were 'screened' on successive days from Monday to Saturday morning. The screening doctor does not see any new patients of his own but continues to see his old patients on return visits. Referrals are also made directly from clinic to clinic but all new patients or patients with new complaints are seen in screening.

A procedure of financial screening on a voluntary basis is carried out and patients able to pay more than the subsidized rate in the clinic are asked to return to the private medical clinic run in the hospital by members of the attending staff. Most of the patients come to the clinic of their own accord and only 23 patients of my group of 140 had letters from referring doctors. Three others had letters from referring welfare societies.

It is interesting here to consider the growing importance of the outpatient

clinic. With many diagnostic facilities available, investigations can be completed on a number of patients who previously would have had to be admitted. Organization is important and at Washington University a full-time clinic administrator was employed with great advantage. As hospital care is expensive, it is an advantage to have many tests done before admission. The organization of a clinic entirely independent of the hospital service, however, has disadvantages. The old Scottish system of a medical firm with its own outpatient clinic and its own wards has a lot to recommend it.

Throughout the year the assistant resident runs a clinic of his own, called the follow-up clinic. When a patient leaves the ward and has no home doctor to return to for follow-up care, the assistant resident may refer any of his patients to his follow-up clinic in order that he may study the long-term natural history of the diseases which he is treating. If the patient presents a problem which is best followed in a special clinic the assistant resident may, if he chooses, refer the patient to such a clinic. Some of the assistant residents spend two years in the one hospital, which provides a fairly adequate follow-up on many of the illnesses.

One intern is assigned to deal with urgent medical problems in the clinic emergency room. As well as the assistant residents there are six attending physicians who supervise two students each. These students take the history and do the physical examination on one patient each and then are checked by the attending physician—a full-time or part-time consultant physician who 'attends' on the ward. The assistant residents see one new patient in the morning and two new patients in the afternoon and between these appointments see five to ten patients on return visits whom they have seen previously. Of a total of 140 patients whom I saw in the clinic in a period of eleven weeks, 31 were admitted to hospital.

At all times there is a senior physician available to give help in cases of difficulty. All patients on arrival at the clinic have a complete blood count, a complete urine examination, a miniature chest film and a serological test for syphilis. These procedures are very useful and in this particular series picked out tuberculosis in 4 per cent. and syphilis in 5.2 per cent. of patients seen.

WORK IN THE WARD

At 08.00 the interns draw blood on the patients requiring investigation. At 08.30 the assistant resident and the intern together make rounds on their patients and may be accompanied by the final-year students. This usually lasts until about 09.30. From 10.00 until 12.00 on Monday and Wednesday the attending doctor makes rounds with the house staff. All patients admitted to the ward must be seen by the attending doctor and this is usually done during the first hour of his rounds. During the second hour of the rounds he pays particular attention to teaching the students. On Friday this period from 10.00 to 12.00 is directed by the professor of medicine and the students present cases to him. Usually two patients are seen during this period.

Throughout the week a number of conferences are held at 12.00. On

Monday interesting x-rays are discussed with the chief radiologist. On Tuesday, a clinico-pathological conference is held in which particular emphasis is placed on the house staff's opinion on the diagnosis and treatment of the patient concerned. Cases are presented by the interns. A history meeting is held on Wednesday. This consists of briefly reading the diagnosis on all patients discharged from the service and then discussing any points of difficulty that arose, any major operations on the service and the necropsies for the week. On Thursday at 09.30 grand rounds are held when diagnostic or therapeutic problems and other interesting cases of the week are presented by the assistant residents to the assembled staff of junior and senior doctors. Some of the consultants come prepared to discuss particular aspects of the disease presented. The discussion, however, is open to any of the students or doctors present and comment is encouraged. This type of meeting encourages the presentation of quantitative data regarding disease rather than imperfectly recollected experience. On the same day at 12.00 a large clinico-pathological conference is held when the cases are discussed by the senior staff of the departments of medicine and pathology. These are taken on wire recording and some of them are published in the *American Journal of Medicine*. On Saturday, at 12.00, there is a lecture by members of the staff for the students but usually attended also by the house staff.

When patients are discharged a summary is dictated by the intern, and the diagnosis is added and coded by the assistant resident. As there is only a limited number of ward medical beds in the hospital (approximately 85), patients are admitted to hospital only when they show a fairly serious degree of illness which is amenable to treatment or is of particular value from a teaching point of view.

TEACHING

A part of the teaching of the students is the responsibility of the assistant residents. Throughout the week they carry out informal sessions with their students. The assistant residents themselves receive teaching from the senior staff in various ways. Some of them, during their free period, work directly under one of the staff members either in an experimental or a clinical capacity. Many of these assistant residents in the year after completion of their assistant residency training may take up fellowships with these same members of the visiting staff. When students have finished six weeks on the ward they are graded on a scale from A to E with plus or minus added to help differentiate them. Notes are made by a secretary of a discussion between the professor, the visiting physician, the resident and the assistant resident, regarding each student. The notes deal with fundamental knowledge, attitude towards patients, initiative, suitability as an intern, and the like. These notes are later used when recommendations are requested. The final year students at Washington University write a report each year which is critical in type and deals with their impression of the teaching they have received. When I was there a radical change in staffing was made at the students' suggestion to improve teaching. The change was

very successful and has been maintained since.

Twice yearly the assistant residents present a series of lectures on medicine to the junior nursing students. A class in physical diagnosis for junior medical students is run in part by the assistant residents. The house staff are encouraged to attend postgraduate meetings, particularly those of the Central Society for Clinical Research held in Chicago in the autumn and those of the Association of American Physicians held in Atlantic City in the spring. The travelling expenses of approximately half the assistant resident staff are paid to each of these meetings.

NIGHT DUTY

Members of the intern staff are on duty on alternate nights and members of the assistant resident staff are on duty every third night. Many of these doctors are married and live out of the hospital except when on duty. When on duty the assistant resident sees all patients coming to the emergency room who are thought to require admission or thought by the intern on duty to need further consultation. He also carries out consultation on the other services of the hospital such as surgery and obstetrics. When he finds a problem which he cannot solve he is expected to ask the resident or his visiting physician to help him.

THE RESIDENT

The resident is in charge of the organization of the medical services directly under the professor of medicine. He is responsible for the work of 8 to 10 assistant residents and 8 to 10 interns. Occasionally, the hospital has two separate services in internal medicine, that is a ward service and a private service, when there may be separate residents for each service. The resident is responsible for the organization of the various conferences throughout the week, for the care and treatment of the patients and for some of the teaching done on the medical service. He is responsible for the consultation service in the daytime with the other specialty services. On arrival in the morning he obtains from the office a list of admissions in the previous twenty-four hours and he visits the wards and patients taking notes on their illnesses. These notes are later discussed with the professor who may himself go and see complicated cases on the wards. Apart from this, the assistant residents are directly responsible for the care of the patients and for calling any necessary consultations. They are guided in this by the visiting physician but the final decisions are made by the assistant resident.

'ELECTIVES'

'Electives' are courses which I had not come across before. In each medical school a certain number of subjects is required for study each year but there is also a number of other courses which a student may take. These may be, for example, on liver diseases, the chemotherapy of cancer or supervised experimental work in one of the university laboratories. Students I have known have been working on the nature of the capsule of torula, the biological assay of vitamin C, and the kidney in experimental shock.

(*To be concluded*)

CURRENT THERAPEUTICS

CXXV.—PHENOXYBENZAMINE

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In 1950 a new synthetic compound, *N*-phenoxy-isopropyl-*N*-benzyl-β-chloroethylamine hydrochloride, was introduced as an effective adrenergic blocking agent. Its approved name is phenoxybenzamine, whilst its proprietary name is 'dibenyline' in Britain and 'dibenzyline' in the United States.

PHARMACOLOGY

This drug is chemically related to, and more potent than, 'dibenamine', is orally effective and is both 'adrenolytic' (capable of blocking the action of circulating adrenaline) and 'sympatholytic' (capable of blocking the effect of sympathetic nerve stimulation) (McLean *et al.*, 1951). Action is at the periphery and, in contrast to the ganglionic blocking drugs, no effect upon parasympathetic impulses is noted. It has been demonstrated that, whilst it is capable of blocking the 'excitatory' functions of the sympathetic nervous system, blockade of the metabolic effects of the sympathico-adrenal system, such as the effect on glucose metabolism or the inhibitory effect on the gastro-intestinal tract, is not achieved. In view of these unique properties the drug seemed ideal for use as a 'pure' sympathetic blocking drug in all instances in which disease might be the result of an increase in vasomotor tone, or arteriolar spasm was believed to play a part.

EFFECT IN NORMOTENSIVE PATIENTS

Subcutaneous or intramuscular injection produces local tissue necrosis and for this reason the drug must be administered intravenously or by mouth. Following an infusion of 1 mg./kg. in glucose and water, over a 20- to 30- minute period of time, or after 2 to 3 mg./kg. orally in a single dose, the following sequence of events occurs (table I). Onset of action varies a great deal from person to person and even in the same individual after repeated doses. Duration of action following a single dose is between 5 and 36 hours. A blockade of sympathetic nerve impulses is established by the following criteria (Moser *et al.*, 1953b).

(1) Partial to complete inhibition of pupillary dilatation; pupils cannot be dilated with 'paredrine'. Homatropine produces satisfactory dilatation.

(2) Nasal congestion indicating blockade of sympathetic vasoconstrictor fibres to the nasal blood vessels; local application of phenylephrine does not appear to relieve the congestion.

(3) Definite diminution of sweating at average room temperature; com-

plete inhibition of sweating as determined by the use of the cobalt chloride 'hot box' technique does not occur.

(4) Postural hypotension and tachycardia. The fall in blood pressure in the upright position is only partially prevented by the use of tourniquets applied to the thighs, but the use of an abdominal binder often decreases this effect. These findings were interpreted to indicate that at least part of

Effects	Time of onset	
	1 mg./kg. infusion	2 to 3 mg./kg. orally
Pupillary constriction	20 minutes	45 minutes
(a) Stuffy nose (b) Diminution in sweating	25 minutes	45 to 60 minutes
Postural hypotension and tachycardia (release of splanchnic vascular tone)	40 minutes	60 to 90 minutes
(a) Blockade of cold pressor response (b) Blockade of intravenous phenylephrine	60 minutes	60 to 90 minutes
Increase in skin temperature and blood flow in upper extremities	45 to 75 minutes	45 to 100 minutes
Increase in skin temperature and blood flow in lower extremities	Not constant with above dose	Not constant with above dose

TABLE I.—Progressive steps of adrenergic blockade with phenoxybenzamine.

the postural blood pressure changes were secondary to a release of splanchnic vascular tone, in addition to some pooling of blood in the lower extremities. A significant fall in recumbent blood pressure does not occur.

(5) A partial inhibition of the blood-pressure rise after immersion of the hand in water at 4°C. (39°F.) for one minute and following 1 mg. of phenylephrine intravenously is noted. The decrease in pulse volume ordinarily noted after these procedures is also blocked.

A rise in skin temperature and an increase in blood flow is observed following the use of phenoxybenzamine, orally or intravenously. Blood-flow increases are less constant in the lower extremities, but some protection against cold stimuli in the lower extremities is noted in patients who have first received adequate blocking doses of phenoxybenzamine. A definite decrease in the effectiveness of the drug is commonly observed after repeated tests.

The major side-effects encountered following both acute and long-term administration of phenoxybenzamine are dryness of the mouth and stuffy nose, transient drowsiness, weakness and fatigue, transient dizziness, palpitations, a decrease in the amount of seminal fluid following ejaculation, nausea and vomiting, and, rarely, tenseness and general irritability.

On the basis of these observations there appears to be definite evidence that phenoxybenzamine produces a fairly effective adrenergic blockade in humans, although a definite delay period is noted following both oral and intravenous administration. (Intra-arterial injection, although effective, does not produce a 'local' effect without systemic manifestations of action.) The delay in action is in contrast to the action of other blocking agents such

as tolazoline, or the ganglionic blockers, hexamethonium, pentolinium, or mecamylamine, with which blockade occurs within a few minutes after administration. It has been suggested that 'dibenamine'-like substances react with a receptor substance in the peripheral tissues and that an equilibrium phase is established before the drug is released. Absorption of oral phenoxybenzamine appears to be complete in some patients, although in others this is not true. Factors of varying absorption may account for varying results reported. A blockade of successive vascular beds apparently occurs, the areas with least sympathetic tone being affected first. The drug does not uniformly inhibit sympathetic nervous system effect on peripheral blood vessels, as evidenced by skin temperature and/or blood-flow responses. Flow increases do not uniformly occur in the lower extremities, especially in patients with an abnormally high degree of vasoconstrictor tone, despite the demonstration of an adrenergic blockade in other areas. Upper extremity responses appear to be more constant. The degree of 'protection' against cold following phenoxybenzamine is not equivalent to that provided by surgical sympathectomy, but is sufficient to produce 'clinical' results. A definite gradual return in vasoconstrictor ability of the peripheral vessels is noted following the continued use of phenoxybenzamine. This also occurs several weeks or months after surgical sympathectomy. This so-called tolerance may represent an adjustment in intrinsic vascular tone.

EFFECT IN HYPERTENSIVE SUBJECTS

In reporting on the effects of phenoxybenzamine in hypertensive individuals, Haimovici *et al.* (1951) reported that a fall in both supine and erect blood pressures occurred in most subjects and that the duration of response was usually between three and five hours following a single oral dose. Some symptomatic improvement was also noted on prolonged administration of 40 to 240 mg./day in four divided doses. Other observers (Corcoran *et al.*, 1952) have reported that, although evidence of a sympathetic blockade has been established, the effects upon blood pressure are minimal, especially in the recumbent position, and that tolerance develops fairly quickly upon continued administration of the drug. Side-effects in all groups of hypertensive patients studied are rarely serious but often annoying; these include weakness, drowsiness, nasal stuffiness and persistent postural tachycardia and 'palpitations'.

Although the intravenous use of phenoxybenzamine generally produces a significant fall in blood pressure in hypertensive individuals, the fall in blood pressure in most instances is not comparable to that following the use of ganglionic blocking agents, such as hexamethonium, pentolinium, or mecamylamine. The duration of fall in pressure is significantly longer, however, after phenoxybenzamine.

RAYNAUD'S SYNDROME

In a comparative study of the use of oral tolazoline, in doses of 100 to 200

mg. daily in divided doses, and of phenoxybenzamine, in doses of 10 to 50 mg. administered three times daily by mouth, with placebo control, it was reported by Moser *et al.* (1953a) that phenoxybenzamine produced the best results in a series of patients with Raynaud's phenomenon. Patients generally noted a decrease in the number, severity, and duration of blanching attacks when this drug was given. The relief of pain was believed to be significantly greater than after tolazoline. Hyperidrosis was definitely decreased. In several cases side-effects proved to be more annoying than the original disease and the drug was discontinued.

Patients without Raynaud's phenomena, but with evidence of cold clammy extremities with sweating, acrocyanosis and hyperidrosis also experienced definite relief upon administration of phenoxybenzamine. In most cases the degree of relief was greater than that following the use of placebos or other available peripheral blocking drugs. Patients with ulceration of a finger or toe and evidence of increased sympathetic nerve activity also obtained good to excellent results following the prolonged use of oral phenoxybenzamine (average dose of 15 mg. three to four times daily). This occurred despite the fact that some 'tolerance to drug effect' developed in several individuals after continuous treatment.

In comparing the results of treatment with oral phenoxybenzamine and intravenous hexamethonium the sympathetic blocking effects of parenteral hexamethonium were found to be greater than those noted after oral phenoxybenzamine (Moser *et al.*, 1953a). It was not believed feasible, however, by the group reporting these findings to continue patients with so-called 'vasospastic' diseases on continuous long-term intravenous therapy. Since the introduction of orally effective ganglionic blocking agents, such as pentolinium, or mecamylamine, additional experience has indicated that generally in normotensive individuals these drugs are as effective as phenoxybenzamine in controlling the symptoms of Raynaud's and associated phenomena. Side-effects of the ganglionic blocking drugs, especially constipation, often limit the use of these more potent drugs.

OCCLUSIVE VASCULAR DISEASE

Results with the use of oral phenoxybenzamine in patients with occlusive vascular disease, but with a large component of increased vasoconstrictor tone, i.e. thromboangiitis obliterans, indicate that a definite release of tone can be accomplished and that clinical improvement will result in many patients if this drug is continued for long periods of time. Although some vascular adjustment rapidly occurs during the first few weeks of therapy symptomatic improvement and rapid healing of ulcerations, if present, are noted in this group of patients. When compared with tolazoline, phenoxybenzamine appears to be more effective, although intra-arterial tolazoline produces superior results when one extremity is involved, and repeated injections are employed (Prandoni and Moser, 1954). Despite the fact that a generalized sympathetic blockade is produced by phenoxybenzamine,

results indicate that in many instances release of vasoconstrictor tone in each extremity is equivalent to that obtained after sympathectomy (Moser *et al.*, 1953b).

In the treatment of patients with arteriosclerosis obliterans without a significant vasoconstrictor component the use of phenoxybenzamine and/or other blocking drugs or ganglionic blocking agents does not produce significant results. In addition, in the older age-group, the use of these drugs presents some danger; consequently, their use is not recommended.

'POST-FROSTBITE SYNDROME'

In approximately 50 per cent. of a large group of patients studied with the 'post-frostbite syndrome' (sweating, burning, or 'pins and needles' sensations and increased susceptibility to cold with hyperidrosis and acrocyanosis) the use of oral phenoxybenzamine produced a definite decrease in sweating and increase in skin temperature and blood flow and a partial inhibition of vasoconstriction following cold exposure. Aching and paræsthesia often decreased. The effect of continuous phenoxybenzamine appeared to be equivalent to that of oral ganglionic blocking agents and superior to that of tolazoline, except when this drug was used repeatedly by the intra-arterial route in cases of involvement of only one extremity.

In another report it was determined that the use of phenoxybenzamine in post-traumatic 'causalgic' states often produced permanent and complete relief of the burning pain characteristic of this syndrome (Fowler and Moser, 1956). In conjunction with the use of ganglionic blocking agents intermittent oral phenoxybenzamine therapy in doses of 60 to 120 mg. a day in divided doses produced in six of twenty-five patients reported permanent relief of causalgic pain equivalent to that previously obtained in other cases only by surgical sympathectomy. Of the remaining group, most had temporary or semi-permanent relief following the use of this drug for short periods of time. In those who did not respond eventual sympathectomy was of no avail. It was concluded that phenoxybenzamine provides a method of predicting the eventual outcome of sympathectomy in causalgia and, in some cases, if the drug is tolerated by the patient, provides a method of definitive treatment of this entity.

THE ROLE OF ADRENERGIC BLOCKING AGENTS

Until the recent introduction of effective sympathetic blocking agents, only limited medical therapy was available to the patient with peripheral vascular disease. Vasodilators previously used in these entities, such as nicotinic acid, papaverine, nicotinyl alcohol, alcohol and histamine, did not consistently prevent vasoconstrictor responses to cold and emotional stimuli. These drugs and tolazoline were occasionally effective but, at best, were temporary and in no way duplicated the effects of surgical blockade of the sympathetic nervous system. With the introduction of phenoxybenzamine and ganglionic blocking agents, effective medical methods of blocking sympathetic nerve innervation became available.

The major theoretical difficulty with the use of drugs which chemically interrupt sympathetic pathways has always been their inability to achieve selective inhibition of one area of the body. Although denervation of one limb might be all that is required, the patient is subjected to a total blockade of the sympathetic system with the possible attendant side-effects of postural hypotension, tachycardia, stuffy nose and weakness. Another disadvantage of this type of therapy, as opposed to surgical denervation, is the necessity for continuous medication. The factor of 'tolerance' to drug effect further limits the usefulness of medical treatment of peripheral vascular disease and other illnesses connected with an increased tone of the sympathetic system. In the case of phenoxybenzamine and the ganglionic blocking drugs this may occasionally be overcome by the use of interrupted therapy or by increasing dosage so that this disadvantage may not be an important one.

It would seem logical at present to reserve the use of chemical sympathetic blocking agents in peripheral vascular disease for the treatment of patients with conditions involving two or more limbs or for those requiring only temporary or intermittent interruption of sympathetic pathways to achieve a satisfactory result. Surgical sympathectomy should probably remain the treatment of choice when permanent denervation of one extremity is required. Drugs such as phenoxybenzamine also appear to be of value when a blockade of the sympathetic system is necessary to determine the degree of abnormal functional vasoconstriction as opposed to organic narrowing of vessels. In cases with a previous surgical sympathectomy and a return of vasomotor tone continuous oral treatment with phenoxybenzamine may also represent the only available effective therapy. In other patients, in whom disease involves both upper extremities, and in whom surgical denervation might have to be more extensive to be effective and less reliable than denervation of the lower limbs, medical therapy may also be a useful procedure.

Intravenous phenoxybenzamine, one milligram per kg. body weight given in an infusion, may be used instead of stellate ganglion or paravertebral blocks in some instances. Although the degree of sympathetic blockade may not be as great as that produced by ganglionic blocking agents such as hexamethonium, pentolinium, or mecamylamine, the longer duration of the blockade produced by phenoxybenzamine is a distinct advantage.

INDICATIONS FOR PHENOXYBENZAMINE

With these considerations in mind, the usefulness of phenoxybenzamine as a clinically effective blocking drug appears to be confined to conditions of increased vasomotor tone such as Raynaud's disease, 'post-frostbite syndrome', conditions of acrocyanosis, or in patients with cold, clammy extremities, hyperidrosis and other manifestations of generalized overactivity of the sympathetic system. In doses of 10 to 100 mg. daily in four divided doses phenoxybenzamine also appears to be indicated in the short-term treatment of patients with thromboangiitis obliterans with ulceration. When

alternated with the use of intra-arterial tolazoline (50 mg. per injection) daily, or the use of ganglionic blocking agents, in normotensive individuals phenoxybenzamine would seem to produce excellent results in the treatment of this type of organic vascular disease with a superimposed 'vasospastic' element. Conditions such as these, in which continuous blockade of the sympathetic system for a short time will achieve a desired result, will often eliminate the necessity for surgical sympathectomy. It is also useful in screening patients for possible response to permanent surgical denervation.

Oral phenoxybenzamine in combination with other blocking agents is effective in the testing and treatment of patients with the syndrome classified as 'post-traumatic causalgia'. In a certain percentage of cases permanent relief will be achieved after continuous medical blockade for several weeks without the need for surgical sympathectomy. It also appears to be a more potent agent than tolazoline and other available peripheral blocking drugs in 'vasospastic' causalgic states, and in many cases of thromboangiitis obliterans. In arteriosclerosis obliterans none of these drugs appears to produce significant results. In the very small group of patients with arteriosclerosis obliterans with a demonstrably significant 'vasoconstrictor' element the sympathetic blocking agents are of value, but in most instances the degree of organic vascular narrowing is severe enough to preclude any increase in blood flow following removal of sympathetic tone, either medically or surgically. The use of sympathetic blocking agents in organic vascular disease should be reserved for acute conditions and for short-term treatment. Because of the frequent occurrence of persistent tachycardia and postural hypotension following effective doses, care should be exercised in using phenoxybenzamine in elderly individuals. Side-effects generally, however, are not severe and phenoxybenzamine is a safe drug to use in normotensive patients, although approximately 10 per cent. of cases are unable to tolerate long-term therapy because of persistent stuffy nose and weakness.

At present there appears to be little indication for the use of oral phenoxybenzamine in the treatment of essential or renal hypertension. Although this drug is effective as an anti-hypertensive agent in some cases, its irregular blood-pressure lowering effects, side-reactions and development of tolerance to its sympathetic blocking action limit its usefulness in long-term treatment. Hydrallazine and the ganglionic blocking agents are more acceptable and more potent as drugs of choice in the treatment of elevated blood pressure from any cause (Moser, 1955). In some instances the use of intravenous phenoxybenzamine in hypertensive crises might be of value, although here, too, other agents are usually more uniformly effective and easier to control. The use of parenteral mecamylamine or pentolinium produces rapid lowering of blood pressure in a higher percentage of cases, and the administration of these drugs can usually be more easily controlled, especially if hypotension is inadvertently produced. Since phenoxybenzamine effectively blocks the action of circulating vasopressor substances these agents cannot be used, except in extremely large doses, to restore blood pressure once an 'over-

shoot' has been produced following its administration. On the other hand, the blood pressure of patients who have received ganglionic blocking drugs readily responds to pressor drugs such as adrenaline or noradrenaline. Hypotensive reactions following intravenous use of these drugs may therefore be easily controlled.

Phenoxybenzamine appears to be of little value as a diagnostic agent in phæochromocytoma, despite its potent blocking effect upon circulating adrenaline. Lowering of the blood pressure or a 'positive test' is 'non-specific' and not diagnostic of a phæochromocytoma, as this response is also noted in essential or renal hypertension. In the preoperative management of patients with a proved tumour, however, the use of oral phenoxybenzamine (10 to 20 mg. four times daily) might be indicated to control blood pressure while the patient is awaiting surgery (Sayer *et al.*, 1954). During the removal of a phæochromocytoma phenoxybenzamine is of little value because of its long duration of action and the delay between administration and effectiveness. Our experience has indicated that phentolamine is a more useful agent in controlling any pressor reactions that occur during surgery for chromaffin tumours.

SUMMARY

(1) Phenoxybenzamine ('dibenyline') is a potent adrenergic blocking agent capable of blocking the effects of both sympathetic nerve stimulation and circulating adrenaline.

(2) Its usefulness in clinical medicine is limited by side-effects, the development of tolerance to drug effect and occasionally irregular action when administered orally.

(3) It is an effective agent for the treatment of peripheral vascular diseases in which an element of increased sympathetic nerve activity can be demonstrated: Raynaud's disease and associated conditions, 'post-frostbite syndrome,' thromboangiitis obliterans, hyperidrosis. It is effective in certain forms of post-traumatic 'causalgic' states.

(4) It has limited usefulness in the preoperative management of patients with phæochromocytoma.

(5) There is little indication for the use of phenoxybenzamine in the treatment of hypertension.

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MINOR SURGICAL PROCEDURES

V.—SUPERFICIAL ABSCESSES

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A DECADE ago many general practitioners carried out their own minor surgery, at times assisted by a colleague versed in anæsthetics. Enthusiasm would appear to have been blunted since the 'Appointed Day'. Even so, many continue to undertake these tasks either on their own premises or (the fortunate few) in the local cottage hospital.

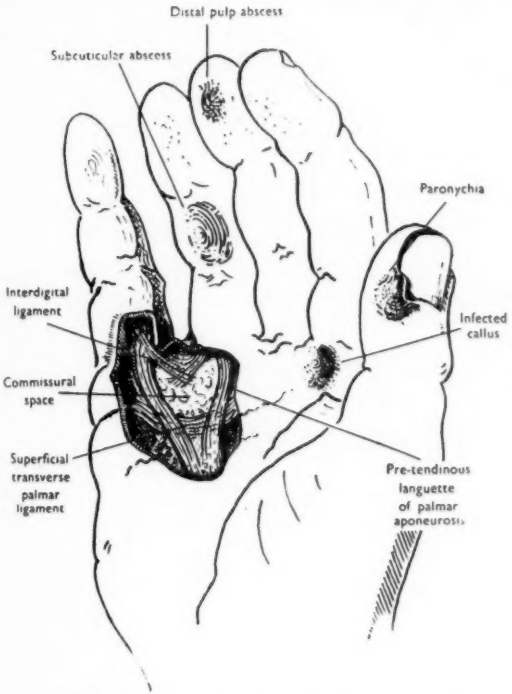

FIG. 1.—Within the commissural space, outlined by 'ligamentous' structures, lie lumbrical muscle, digital nerves and vessels. Spread of infection from an overlying callus or pulp abscess of the digit can readily occur. 'De-roofing' of the central part will drain the space. (Exposure in the diagram is deliberately wide.)

Innumerable conditions may reasonably be listed under the heading 'Superficial Abscesses'. It is with some *commonly* seen in practice that this account will deal, but in detail with only one or two, for space is at a premium.

THE ROLE OF ANTIBIOTICS IN MINOR SURGERY

Timely administration inhibits many an infection. Resolution follows fast. Suppuration is not seen. Theoretically, organism and sensitivity ought first to be determined. Practically, this is a counsel of perfection. Even with the 'broad spectrum' antibiotics, the chance of encountering insensitivity is increasingly common. Nevertheless, the benefit to be derived from their selective use continues

to outweigh the disadvantages, but when antibiotics are regarded as a substitute for surgery, trouble may arise. As an adjunct, they are invaluable, but the old dictum still holds good: 'Where there is pus; let it out'. Early effort must therefore be directed towards resolution and, should this fail, towards the formation of the inflammatory barrier—pyogenic membrane, or abscess wall, call it what you will. Locally then, with traditional remedies the inflammatory response is encouraged, while generally, with chosen antibiotic, an attack is made upon the organism. But, it must be urged, in the case of most surface infections antibiotics should be resorted to only when clinical judgment determines that local defence is inadequate and distant spread is likely. There are, of course, exceptions. The lactating breast is one and the severe hand infection with lymphangitis and axillary adenitis another. A sense of proportion must be maintained, for one is often asked to see a discharging wound with foreign body deep within, or an ingrowing infected toe nail, the patient having been 'on penicillin for two weeks—does not seem to settle. ?Surgery'.

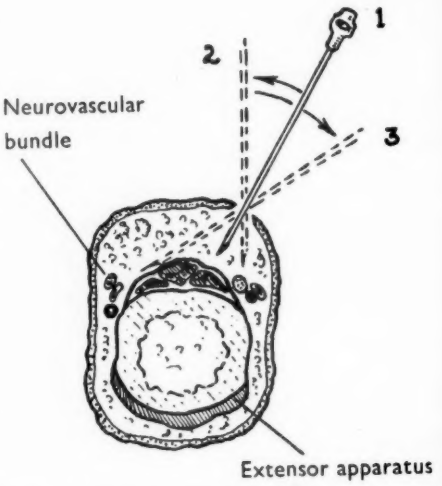

FIG. 2.—A section through the proximal segment of the digit to show the method of local infiltration.

HAND INFECTIONS

The general practitioner, by recognition and treatment of early hand infections, can do much to reduce morbidity and economic loss. Most cases can readily be tackled *ab initio* in the practice, but responsibility for tendon sheath infections and those of the cellular spaces of the hand is best shared with the hospital. Four examples will be taken (fig. 1):—

(1) The pulp infection of the distal segment.
(2) The pulp infections of the middle and proximal segments.
(3) Paronychia.
(4) Infection of the commissural space.

The basic armamentarium ideally should be:—

A table across which doctor and patient may face each other.
A good light of the 'anglepoise' type.
An upturned gallipot on which the patient rests his hand.
Two gallipots—the first containing acriflavine, chlorhexidine or other antiseptic;

the second with glycerin-magnesium sulphate paste, clear and not too viscous, so that it runs easily.

Sterile wool and gauze.
Local anæsthetic (2 per cent. procaine or lignocaine), syringe and needles.
Fine rubber finger-tourniquet.
Watson-Cheyne dissector.
Pair of sharp pointed scissors.
No. 15 Bard Parker blade and handle.
Fine toothed dissecting forceps.
Spencer Wells forceps.

Method.—Clean the base of the finger with antiseptic, then once round with the tourniquet and clip with Spencer Wells, under a slight degree of tension. Now inject the 'local'—5 to 10 ml. into the lateral aspect—working it slowly towards the other side (fig. 2). Tension is developed and cyanosis of the digit follows. Avoid the nerve and vessels at 2 and 10 o'clock and *never* use solutions with adrenaline, or irreversible digital arterial spasm may then occasion gangrene. Observe the patient's colour at this juncture—there are one or two who faint. Now leave him for ten minutes and the operation may begin.

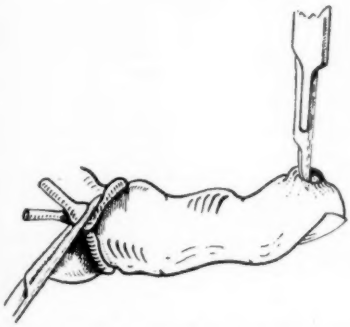

FIG. 3.—The tourniquet applied and nature of approach to distal pulp infection.

DISTAL PULP INFECTION

Do not wait for fluctuation. Find the point where tenderness is maximal. Your index covers too much ground, so use the Watson-Cheyne. Remove full thickness skin with a No. 15 blade held vertically (fig. 3). A circle, ¼ of an inch (6 mm.) across, will often suffice. With the probe then loosen gently all the damaged tissue. The feel of normal pulp is unmistakable. A wisp of gauze roll soaked in glycerin-magnesium-sulphate paste is then applied and a temporary dressing: 'temporary', for bleeding is quite free with the tourniquet released, and more fresh wool goes on before the patient leaves. Thereafter a daily change of the glycerin-magnesium-sulphate dressing is all that is required. The days of 'hockey stick' incision are, or should be, over, although neglected cases, with destruction far advanced, demand more radical exposure. Send them to the consultant—*not*, please, to the junior casualty officer!

PULP INFECTIONS OF MIDDLE AND PROXIMAL SEGMENTS

Similar to distal pulp infections, these differ in one anatomical respect: fibrous tissue septa confining distal pulp infection are absent in the proximal two-thirds of the finger (fig. 2, 4, 5). Localization is less certain and spreading cellulitis may occur. Organisms readily attain the diffluent fat of the com-

missural space or that around the lumbrical, called the 'lumbrical canal', and so by either pathway may gain access to the palm.

Attack these pulp infections early, as you would the distal segment, and do not hesitate to 'de-roof' widely all volar skin if need be. It is surprising what little scar remains when healing is complete, for in the hand (as over ischio-rectal fossa) skin grows thick and fast to close the widest gaps.

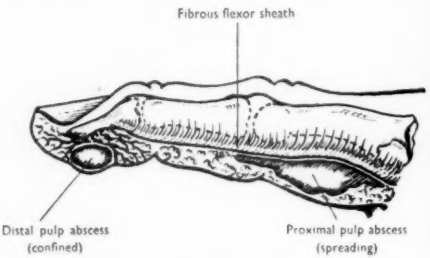

FIG. 4.—A diagrammatic finger to contrast the proximal and distal abscesses of pulp.

COMMISSURAL SPACE INFECTION

Arising from infected callus or a scarce-noticed penetrating wound by thorn, wood splinter, steel wool and the like, localized abscess in the web is common, or the infection spreads, as has already been noted, from the infected finger (fig. 1). The principle of early drainage still holds; the anæsthetic is a problem. A nerve block at the wrist appeals to few, whilst a general anæsthetic may not be readily forthcoming. But if the overlying horny skin be gently sliced away, with the knife held flat upon the palm, until capillary ooze is seen, the ethyl chloride spray becomes effective. Direct it on the part till sudden whitening betokens anæsthesia. Then, as before, remove whole thickness roof.

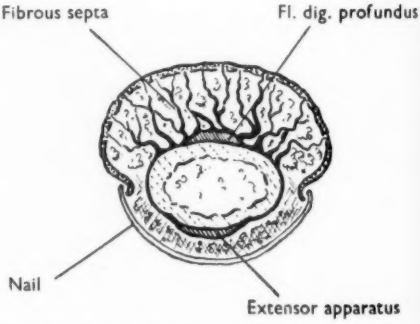

FIG. 5.—A section through the distal segment of the digit showing the density of fibrous septa in the pulp. (Compare with fig. 2.)

PARONYCHIA

With the flat end of the dissector, or with the help of the point of a No. 15 blade, the nail fold is raised up (fig. 6). The pus must then be followed until the abscess wall is reached, for it will track round to the sides and on to the dorsum of the finger, over the root of the nail. All can be exposed by careful elevation without recourse to vertical incisions or raising dorsal flaps. Adequate exposure at this stage avoids the ugly ridging and deformity of the nail that follows chronic sepsis, and indeed may save its loss. Before the dressing is applied, snip off all skin of the nail fold whose vitality is doubtful. If in the later case, the pus is seen to track beneath the

nail, pocketing between its root and bed, then the root must go or the infection smoulders on. The root by then is often soft and pliable and scissors passed from side-to-side effect its quick removal. Leave the distal

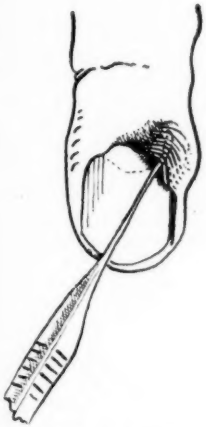

FIG. 6.—Mode of elevation of the nail fold in paronychia.

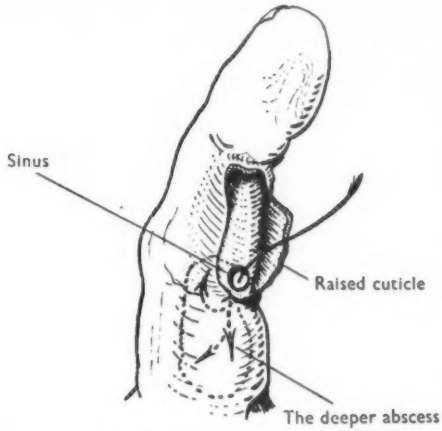

FIG. 7.—The subcuticular abscess has been drained. A sinus in the dermis leads to an abscess on the fibrous flexor sheath. (Compare with fig. 4.)

two-thirds of the nail as cover for the exquisitely tender tissue underneath. Its painless separation will occur as new nail grows when healing is complete.

SUBCUTICULAR INFECTION

The subcuticular infection is as common as those deep to whole skin just described. The surgical approach is much the same but be on guard for 'collar stud' effects, for many subcuticular collections betoken an infection deep within. Remove the damaged cuticle completely and inspect the dermis for the sinus that may lurk beneath the edges of the wound (fig. 7). Then lay all widely open as before. It is in the hands of industrial and agricultural workers that this condition is most usually encountered.

THE 'COLD' NECK ABSCESS

Patients suffering from this condition will normally be sent for specialist opinion, when streptomycin, PAS and isoniazid therapy precedes a major surgical attack upon the glands. Many, however, first present with 'collar stud' infections and well advanced signs of fluctuation. Oft-times the overlying skin is thin and cyanotic, or red and angry, with little that is 'cold' about it, and early rupture threatens. Doubts as to the accuracy of diagnosis often arise. Much can be done to save the threatened skin: deny access to pyogenic organisms; confirm the diagnosis and relieve the pain.

Method.—A local anæsthetic is instilled through healthy skin an inch

(2.5 cm.) or more beyond the lesion (fig. 8). Tension is maintained towards the latter so that the final needle track will be oblique. The needle is then made to change direction and to advance until the wall of the abscess cavity is reached (infiltrating anæsthetic all the way) and then withdrawn. The widest bore of needle, extra sharp, is then employed, and with the index finger at the estimated distance from abscess cavity to skin, it is pressed home along the anæsthetic track. A definite resistance will be felt as the abscess wall is pierced (fig. 9). Now there may be aspirated creamy pus or caseous material, the latter not without some difficulty. With needle still *in situ*, a fresh syringe is used and streptomycin, 1 g. in solution, is injected, saving a little for the needle track.

FIG. 8.—A method of approach for threatened rupture of 'cold' abscess of the neck. The situation of the carotid sheath should be remembered. An approach behind the abscess may often be preferred.

The process is repeated weekly, or more often, until quiescence is achieved. If by chance the pus is non-tuberculous, incision of the abscess in the usual way is called for. A search should then be made for a focus of infection, such as tooth or tonsil, bearing in mind that pediculosis capitis is sometimes the offender.

BREAST ABSCESS

There are three situations in which fluctuation should *never* be awaited—the pulp of the finger, the breast, the ischio-rectal fossa. Overlying dense loculated fat and normal structures may render fluctuation late.

If, in the breast, by inappropriate or inadequate antibiotic therapy, the fire be

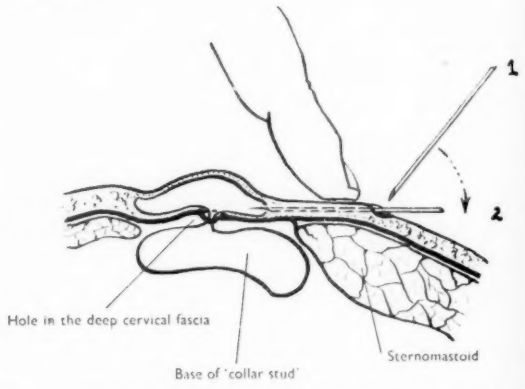

FIG. 9.—The pathway taken by the aspirating needle in 'cold' abscess of the neck. It does no harm to pierce the sternomastoid or deep cervical fascia, entering the deeper portion of the 'collar stud'.

dampened down, but smoulders on, much glandular destruction will occur. Persistent pain and tenderness, malaise and spikes of fever, and a tender gland or two in the axilla, even in the absence of the signs of fluctuation, call for exploration. The findings in such cases are disturbing. The

FIG. 10.—Obtaining dependant drainage in a breast abscess that has 'pointed' above the nipple.

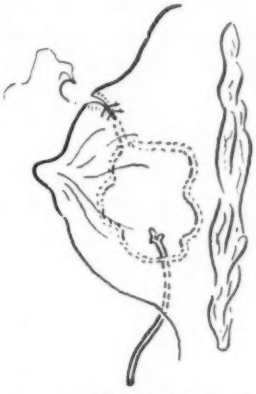

FIG. 11.—High incision was dictated by the nature of the lesion. The pus has been evacuated; dependant drainage secured and the exploratory wound is being sutured.

pyogenic membrane seems unduly thick; much of the breast is seen to be involved; a disproportionate amount of pus is found and yet laboratory examination may well reveal attenuated organisms, insensitive to the antibiotic. It follows that in every case in which an immediate response (to penicillin, say) is not obtained, early operation must be offered.

Method.—A general anæsthetic is essential. The skin incision is centred over the point of maximum tenderness, and of a size sufficient only to admit a forceps and exploratory finger which, plunged into the cavity, disrupts the walls of loculi (Hilton's method it was called). When possible, the incision should parallel the edge of areola. Few vessels are encountered with incisions of this size and the cosmetic end-result is good. The larger abscess cavities, as in the 'penicillin breast', respond most gratifyingly to further measures. Evacuate the pus, then pass a forceps through the most dependant part of the cavity beneath the skin of the breast. With jaws a little open, incise the skin between, then, grasping the smallest size of self-retaining catheter, withdraw (fig. 10). The exploratory wound is stitched and the catheter is allowed to drain into a fold of gauze (fig. 11). Thereafter, irrigate twice daily with warm normal saline and introduce a quantity of tryptic ferment in solution, spigotting the catheter until the next attendance. Streptokinase and 'trypure novo' are effective. Much necrotic debris comes

away and the method hurts the patient not at all. High breast incisions, visible in evening dress, then heal with little scar and convalescence is considerably shortened.

Lactation presents an added difficulty for tension is increased and milk is a welcome pabulum for pyogenic organisms. Twice or thrice daily stilbœstrol, 5 mg., will bring about cessation, although its use must be continued for ten days at least. For those who cannot tolerate the drug, ethinylœstradiol offers a welcome substitute. Rarely, in the breast with immediate response to penicillin therapy alone, breast feeding may continue, but milk from the infected side must be discarded, and supplementary feeding may be called for.

'STITCH' ABSCESS

An infected hæmatoma or buried non-absorbable material, or both, determine the appearance of a superficial abscess in an operation wound, 'clean stitched' and seemingly free from all infection when the hospital 'inpatient' was returned to the care of the general practitioner. Even such absorbable material as plain catgut is commonly at fault. More resistant to treatment and often needing readmission are those with wounds wherein deeply buried nylon thread, floss silk or the like, occasion deep infection, presenting as a superficial abscess which does not respond to treatment and proceeds to form a chronic sinus. In the majority, however, the management is simple.

Method.—The new-healed wound is relatively painless and if the exploratory blade is made to cut precisely in its length, no anæsthetic is required. An area, raised and softened in the scar, with thin, unhéalthy-looking covering, determines accurately the centre of incision. As a rule the foreign body will be discharged with pent-up pus. If not, a gentle search with Spencer Wells forceps will often draw it forth. It should be observed, however, that some discharge continues until *all* foreign and unhealthy matter is extruded. Prolonged discharge, or healing and then breaking down on several occasions, suggests that the mischief is more deeply seated, and the surgeon who performed the operation should be consulted.

CONCLUSION

Much more remains to be discussed. Of necessity, many conditions with which the general practitioner might deal have been excluded. These new examples may suffice, however, to interest those who hitherto have not attempted surgery, and may suggest to others a new approach to some old problem.

To Mr. Hugh F. Anderson,of St. George's Hospital, London, I would record my thanks. It was from him that the method and experience were gained in dealing with infections of the hand.

REVISION CORNER

BRADYCARDIA

BRADYCARDIA, which is Greek for slow heart, is applied to heart rates of less than 60 per minute. Care must be taken to distinguish between the true heart rate and the rate as judged by feeling the radial pulse. According to the rate and underlying mechanism, the condition may be very serious or, as is usual, of no importance.

SINUS BRADYCARDIA

This is the commonest form. The heart beats in the normal manner, and the bradycardia is due to a slow rate of discharge from the sino-auricular node. It is not uncommon in healthy middle-aged or elderly people, and also occurs in a younger age-group amongst athletes. With exercise the rate increases in a normal way. As a manifestation of heart disease it is seen as often as tachycardia in the acute stage of some cases of cardiac infarction, and recovered cases also may show a persistently slow pulse at rest. In the acute case there may be extreme sinus bradycardia: in one of my cases the rate was 33 per minute sinking to 24 per minute and leading to faintness. Other conditions accompanied by bradycardia are cerebral compression, severe jaundice, digitalis and morphine effects, and convalescence from acute infections. The pulse may be rather slow in myxœdema, but this is not to be relied upon in diagnosis as the rate may be normal, especially in younger subjects who may have hypothyroidism after thyroidectomy or from the effect of an anti-thyroid drug. The dying heart shows extreme bradycardia, slowing progressively until it finally stops.

Most cases of sinus bradycardia can be recognized by an exercise test which causes acceleration, deep breathing which causes increased rate during inspiration, and watching the venous pulse in the neck which is of normal appearance and synchronous with the arterial pulse.

HEART BLOCK

In the usual form of heart block leading to bradycardia the rate is likely to be between 30 and 50. The lesion is in the atrio-ventricular node or the bundle of His, which is unable to transmit any impulses from the auricle—complete block; or only alternate impulses—2:1 block. By looking for four signs it is sometimes easy to recognize these abnormal rhythms without an electrocardiogram. (i) In complete block the rate does not increase with exercise and this test should be carried out unless contraindicated by the patient's condition. (ii) Listening at the apex usually reveals a diagnostic sign. This is a variation in the intensity of the first sound so that mostly it

is very faint but every now and then is loud and sharp. This sign is caused by the changing time relation between auricular and ventricular contraction. (iii) Another sign sometimes heard at the apex is an audible atrial contraction, a faint muffled sound heard in the long diastoles. (iv) The pulsations in the neck may give a valuable clue, the venous and arterial pulsations being independent and the former much quicker than the latter. Also there is occasionally a large venous pulse, a result of simultaneous auricular and ventricular contraction. In 2:1 heart block the pulse rate may increase with exercise, and inspection of the neck will reveal a venous pulse twice the rate of the arterial.

RARER CAUSES OF BRADYCARDIA

Nodal rhythm.—When the activity of the sino-atrial node is depressed the heart beat is stimulated by the atrio-ventricular node. This is called nodal rhythm and the rate is usually between 40 and 60. The impulse to contraction may arise in various parts of the elongated node, but in any case the impulse ascends to the atrium and descends to the ventricles and their contractions are more nearly synchronous than with normal rhythm. When actually synchronous a large venous pulse occurs in the neck. The usual causes of nodal rhythm are ischæmic heart disease and excessive digitalis action.

Sino-atrial block.—This is a rare cause of bradycardia. In 2:1 sino-atrial block alternate impulses from the node fail to reach and stimulate the atrium, so that the heart rate is halved exactly. It has to be differentiated from extreme forms of sinus arrhythmia in which the cycle may almost double in length during expiration. The usual causes of sino-atrial block are ischæmic heart disease, digitalis and quinidine.

False bradycardia.—Sometimes the radial pulse feels slow but it is not giving a true measure of the heart rate and it is necessary to guard against the mistake of calling this bradycardia. The deception is commonest when there are multiple extrasystoles and particularly when these occur every other beat. The pulse wave of the extrasystole may be too feeble to be felt at the wrist or, though present, may be missed without careful palpation. Thus, with alternate extrasystoles and a heart rate of 80, the pulse is counted as 40. Less often, in the various forms of tachycardia many of the beats are so small that only a small proportion are felt at the wrist. In atrial fibrillation the peripheral pulse rate cannot be relied on as a measure of the heart rate; in this arrhythmia it may happen that the higher the ventricular rate the less the pulse rate. In all these false bradycardias the true rate is of course apparent on listening to the heart.

TREATMENT

For sinus bradycardia of moderate degree, and this includes the great majority of cases of slow heart, no treatment is called for. For the exceptional

case of extreme sinus slowing, a sympathetic stimulator such as ephedrine, ½ grain (30 mg.) by mouth, or the intramuscular injection of methylamphetamine, 10 mg., can be used—though cautiously if cardiac infarction is the underlying cause. When digitalis is the cause of undue slowing in either sinus rhythm or atrial fibrillation, or seems responsible for sino-auricular block or nodal rhythm, it should be omitted for a time. The same applies to abnormal conduction due to quinidine. Heart block will usually only call for treatment in the complete form when severe bradycardia is giving rise to symptoms. Then injections of adrenaline (1:1000), 5 to 10 minims (0.3 to 0.6 ml.) intramuscularly, are the most effective treatment. For more prolonged effect adrenaline in oil can be used. In ventricular standstill adrenaline has been injected into the heart, and a machine to apply electric shocks to the precordium has also been used to restart ventricular contraction.

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Physician, and Physician in Charge of the Cardiac Department, Poole General Hospital.

PARAPHIMOSIS

IN this condition the retracted prepuce cannot be restored to its normal position. Most normal prepuces, when fully retracted, reduce themselves, but phimosis (tightness of the foreskin) is a relatively common condition and is caused by chronic inflammation of the prepuce (balanitis), which in itself is caused by the irritation of infected smegma following poor hygiene. If the prepuce is in any way tight, constriction occurs due to cutting off of the venous return of the prepuce and even, in time, of the glans. This results in discomfort due to œdema, which occurs rapidly and the mucosa of the foreskin swells, thus making the constriction ring even tighter and a vicious circle is set up. An intelligent, fully conscious or non-uræmic adult will soon notice what is wrong and reduce the prepuce with rapid relief. It is surprising, however, how often these conditions are not fulfilled and the condition progresses to irreducibility, causing great pain and œdema and, in very rare instances, even sloughing.

ETIOLOGY

In youth the condition is seen after sexual intercourse following alcoholic excess. In his semi-anæsthetic state the unfortunate victim forgets to replace the prepuce, as the warning of pain is absent until the condition is too severe for him to help himself.

In the aged the prepuce is drawn back to allow for adequate cleansing of the glans as a preliminary to instrumentation (cystoscopy or passage

of a catheter). When the medical attendant has completed his treatment or investigation he may forget to restore the prepuce to its normal position.

Paraphimosis is extremely rare in children. This is because a normal baby's prepuce may not be fully retractable until the age of 2 and there should be no call to retract it forcibly. For the condition to occur at all, the foreskin must be retracted right behind the corona and parents rarely inflict this upon their offsprings, realizing that gentle partial retraction and cleansing with plain water is all that is required.

It is sometimes stated that phimosis is commonly congenital, but for this to be so there must be a pinhole opening in the prepuce which balloons out with urine on each occasion that the child micturates: this is rare as a congenital condition, but may occur in older babies secondary to a napkin rash caused by decomposing urine. This would be an indication for circumcision, but is rarely, if ever, a cause of paraphimosis as the child screams the moment retraction is attempted.

It cannot be overemphasized that a long foreskin which cannot be fully retracted is not an indication for circumcision in the newborn. Provided that it can be withdrawn painlessly to see the external urinary meatus which is clean, and free from redness or ulceration, the child is normal and there should be no interference—merely sensible but minimal hygiene, careful drying and no powdering, as the latter clogs and irritates.

TREATMENT

Treatment depends upon whether the condition is (a) mild, (b) moderate, or (c) severe.

Mild cases.—The penis is grasped in the hand. All the fingers and thumb of the other hand are then used to squeeze and elongate the glans in order to compress it under the constriction ring—the other hand eases the skin of the shaft of the penis over the glans. The classical method using two fingers and the thumbs of each hand fails because this tends to spread the glans, making reduction impossible. This technique is likely to fail except in early mild cases.

Moderate cases are treated by the injection of hyaluronidase: one ampoule is broken open (1,500 international units) and this is dissolved in 4 ml. of 1 per cent. plain 'xylocaine'. It dissolves immediately in a much smaller quantity of fluid. I prefer a local anæsthetic to sterile water in making the solution—for obvious reasons. It is completely harmless and an aqueous hyaluronidase injection is painful. The injection is made in four sites 'around the clock' into the œdematous mucosal ring which is so characteristic of the condition. The swollen parts are then wrapped in gauze which has been wrung out in iced water. Other solutions on the gauze (e.g. adrenaline) are, in my experience, useless. After ten minutes, almost magically, most of the swelling will have disappeared and reduction is performed simply, quickly

and painlessly in most cases. 'Hyalase' is an excellent preparation of hyaluronidase which has the added merit of being British. This treatment can sometimes be adopted even in children but, if the condition has occurred in a child and reduction is impossible except under anæsthesia, it is often wise to send the patient to hospital for further treatment under a general anæsthetic.

The *severe type*, in which the œdema is massive and the constriction ring very tight, may not respond to this measure, but nothing has been lost in attempting it: in fact, the opposite, as some anæsthesia has been obtained.

A soft rubber catheter is placed around the base of the penis and held in position by a hæmostat to act as a *venous* tourniquet. In other words, it need not be unpleasantly tight and is used merely to confine the local anæsthetic to the area. Two per cent. plain 'xylocaine' is then injected subcutaneously as a ring block right round the circumference of the penis distal to the tourniquet. Hyaluronidase is *not* used in this solution. The 'xylocaine' must be plain and contain no adrenaline (occasional gangrene of digits has been reported with adrenaline, but never with plain anæsthesia). About 6 ml. of solution are used. Anæsthesia of the penis is complete in five to ten minutes. A simple, quite safe method of circumcision is now performed.

With scissors the œdematous mucosal ring is cut away completely, except in the mid-ventral line, so as not to injure the frænal artery until it has been occluded by a stitch later in the operation. After this the constriction ring behind the corona can be seen and felt to be very tight. It is grasped with forceps inserted under the edge and cut in one or more places. The cut or cuts are only just enough to relieve the constriction ring. Now the skin can be pulled down quite easily. A small collar of skin (the constricting part) is next cut away and the edge united to the cut edge of mucosa by a few interrupted catgut sutures. A mattress suture unites the mucosa and skin to underrun the frænal artery which is now cut ventrally. A few turns of ribbon gauze are now wrapped around the area and from a dropper a little compound tincture of benzoin B.P. is used to moisten the gauze. The tourniquet is removed.

The patient is kept in bed for a few days and adults are given analgesics for twenty-four hours and stilbœstrol, 5 mg. thrice daily for four days, to prevent erections which would be painful and cause the few stitches to be pulled out.

This operation is easy to perform, safe and extremely satisfactory. A dorsal slit should never be performed. It is an untidy operation and circumcision is always needed later which doubles the inconvenience to the patient. The dangers of infection following immediate circumcision have been greatly exaggerated, and it is doubtful whether even an antibiotic cover is called for. The dressing is changed daily after a bath. Paraffin gauze is avoided as it makes the area soggy and delays healing.

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NOTES AND QUERIES

Treatment of Parkinsonism

QUERY.—I would be most interested to hear of any recent advances in the treatment of Parkinsonism. In particular I have heard of 'supersonic' vibrations in a 'narrow ray directed to the affected parts of the brain' which I am told is being used in America. I have a patient of high intelligence who has responded well to benzhexol four times a day and is keen to return to a responsible office job. As he did not do well on belladonna and stramonium mixtures, I am reluctant to push the benzhexol to the stage of producing side-effects. What might be considered a safe maximum dose, and what side-effects are usual?

REPLY.—For many years neurosurgeons have carried out operations to reduce the disability of Parkinsonism. At first these consisted of removal of parts of the motor cortex, or division of the pyramidal tract either in the midbrain or the spinal cord. These operations sometimes abolish both rigidity and tremor but often replace them with paralysis. In the past few years they have been replaced by a totally different procedure, the basis of which was discovered by accident. At the time of writing, this operation, known as chemical pallidectomy, consists of introducing a needle into the globus pallidus (a structure which is always involved in Parkinsonism) and injecting some destructive fluid, usually alcohol. This is not a very difficult procedure for the neurosurgeon and is often followed by quite remarkable results, particularly abolition of rigidity in the opposite limbs. The procedure is still too new for any form of final assessment, and in particular it is impossible to say whether the results will last for years or perhaps for ever, and of course the procedure is not entirely devoid of risk. The use of supersonic irradiation in the United States is designed to damage the globus pallidus in the same way, but I have had no personal experience of this procedure.

Modern drugs have largely replaced belladonna and stramonium. Benzhexol is sold in tablets of either 2 or 5 mg. The dose should be steadily increased until toxic symptoms arise, and should then be slightly reduced and continued at that level. The commonest of these symptoms is dizziness. The maximum dose varies considerably—partly according to the patient's weight—but a person of average build will usually take from 15 to 20 mg. a day and, as with all drugs, the best results follow the use of maximal intake. An important part of the treatment of Parkinsonism is the use of vigorous active physiotherapy.

HUGH GARLAND, T.D., M.D., F.R.C.P.

Treatment of Localized Scleroderma

QUERY (from a reader in Cyprus).—I would be grateful if you could give me some information about the treatment of localized scleroderma. In the case of my patient, a woman aged 35 years, it appears as a band ¼ inch (0.5 cm.) wide and 2½ inches (6.5 cm.) long in the region of the right clavicle.

REPLY.—There is no satisfactory treatment for localized scleroderma (morphœa). The patch could certainly be excised but, in view of the dimensions, it is unlikely that the cosmetic result would be any better than at present. Morphœa gradually becomes less noticeable and becomes softer over the years.

O. L. S. SCOTT, M.B., M.R.C.P.

Inoculation Before Emigration in Infancy

QUERY.—A baby who will be six months old in May, and a seven-year-old boy, will then be travelling by sea to Australia. What inoculations are essential for the baby and what dosage? Vaccination against smallpox will be done. She has recently had broncho-pneumonia. Are there any other points of medical interest in this connexion?

The boy was vaccinated and immunized against pertussis and diphtheria in infancy. Revaccination against smallpox was done one month ago. A two-dose course of poliomyelitis vaccine will be available in a few weeks. Can and should TAB be given as well? It is recommended by the shipping line.

REPLY.—In the case of the baby I suggest the following schedule:—

Smallpox vaccine, as soon as convenient. Three weeks later, diphtheria-tetanus-pertussis prophylactic (first dose). Four weeks later, diphtheria-tetanus-pertussis prophylactic (second dose).

In view of the recent history of broncho-pneumonia, early protection against pertussis is all the more advisable. Pertussis vaccine is a constituent of triple prophylactic, which is alum-free and does not carry an undue risk of associated poliomyelitis.

It will not be possible to complete any programme of essential inoculations before the baby travels to Australia by sea. On arrival she should be immunized further with a dose of triple prophylactic—the doctor concerned will probably wish to select the preparation. The first two doses of a course of poliomyelitis vaccine would also be required soon afterwards, at an interval of three to six weeks. The volumes to

be injected are in the direction leaflets of the various products.

At the age of twelve to eighteen months, the child should receive reinforcing injections of triple prophylactic and poliomyelitis vaccine. I have not included BCG, as this vaccine is not ordinarily required.

I doubt the necessity of giving TAB vaccine to the boy, as the water supply on board ship and in the cities and larger towns of Australia is almost certainly above reproach. The shipping line may have advised this vaccine on account of the possible risk of contracting typhoid or paratyphoid in remote districts of Australia, or at unhygienic restaurants in ports of call. The risk of infection is seldom great, and several of my colleagues have visited Australia without receiving a course of TAB vaccine. Moreover, the modern treatment of the enteric fevers with antibiotics has reduced appreciably the period of disability from these diseases. Whether it is decided to proceed with prophylactic immunization or not, unnecessary risks should not be run with food and drink in any area where intestinal infections may be endemic.

A child aged seven years could receive doses of 0.2 and 0.4 ml. of ordinary-strength TAB vaccine, spaced by at least seven to ten days, but preferably twenty-eight days. A third dose of 0.4 ml. should be given about six months after the second. The schedule is modified if febrile reactions are marked. The individual doses of the course should be separated from those of poliomyelitis vaccine by about three weeks, in order to reduce the likelihood of any immunological interference between responses to the different antigens.

As the boy has not received any diphtheria immunization since infancy, I recommend a boosting dose some time this year, and I also suggest active immunization with tetanus toxoid. Although the inoculation programme seems heavy, tetanus immunization might be more important than the proposed TAB vaccinaton.

A personal immunization card should be made out, if this child does not possess one already. It should be kept with the utmost care, but made readily available when inoculations of all types are given or when an infectious disease is contracted.

H. J. PARISH, M.D., F.R.C.P.ED.

Cranial Arteritis

QUERY.—I would be grateful for some information on temporal arteritis. In the past six months I have had in my practice three cases—all in elderly females. Never having seen a case before, I missed the diagnosis in the first patient and she went blind in both eyes. The second lost the sight of one eye. Forewarned by these disasters, when the third case occurred I immediately sent her into hospital where she was treated with anticoagulants and prednisolone and has retained her sight unimpaired.

None of my textbooks mention the condition and I should be grateful for information on the etiology, prognosis—particularly with regard to the frequency of eye complications—and treatment. For how long does treatment have to be maintained?

REPLY.—This condition is better called cranial than temporal arteritis as lesions are by no means confined to the temporal vessels. It is, however, in these that clinical evidence of the condition, with swelling and tenderness, is most easily detected. The incidence occurs most heavily in elderly women. The intensity of the pain of which sufferers with this condition complain is probably as good a pointer to the condition as any, and should lead to careful examination of the temporal vessels and those in the occipital region.

Blindness is unfortunately common and usually permanent. It occurs in about one-third of the patients. The etiology of the condition is quite unknown, although the histological appearances show that it is due to a subacute inflammation of the adventitia spreading into the media and leading eventually to thickening of the intima. Giant cells appear in the media, together with lymphocytes and plasma cells. Thromboses are quite common. The changes are not, in fact, confined to the cranial vessels, and the condition is sometimes referred to as large-vessel polyarteritis.

Treatment by anticoagulants and steroid hormones generally results in rapid symptomatic relief but may not prevent the development of blindness. The length of the treatment must be determined for each individual case, but will probably lie between six weeks and three months in most of them.

J. S. RICHARDSON, M.V.O., M.D., F.R.C.P.

Cousin Marriages

QUERY.—Could you give me the current opinions for or against marriage between first cousins in so far as this might endanger the health of their offspring?

REPLY.—The difference, from the genetic point of view, between a marriage of blood relatives and a marriage of unrelated people is very simple in principle. Harmful recessive genes are widespread in the population and in all probability each of us carries at least one or two. With the great majority of marriages husband and wife carry different recessive genes, and the children are normal. Occasionally, however, husband and

wife happen to carry the same harmful gene. Should a child receive the same harmful gene from both parents—the risk of this happening is 1/4—then he will suffer from one of the numerous, though fortunately rare, recessive abnormalities.

Blood relatives have some of their genes in common, having received them from the same source: for example, with first cousins the proportion is one-eighth, hence in such a marriage there is a definitely increased risk that both parents will tend to carry the same harmful gene, with the further chance that both will pass it on to a child. This is the increased risk inherent in the marriage of blood relatives. There can be no doubt about this increased relative risk, but what interests the individual is the absolute risk, and provided that no recessive defect has already appeared in the family, the absolute risk, though larger than with an unrelated marriage, is probably still quite small. It is certainly much smaller than the chance of hæmolytic disease in a second or subsequent child when a rhesus-negative woman marries a rhesus-positive man, which is what happens in about 15% of all marriages. So that although there is a greater chance that some undesirable recessive or other will turn up, it does not seem to be so big a risk that sensible people knowing the facts need let it outweigh other considerations favouring the marriage.

Two further points should be made. The first is that an appreciably increased chance only applies in the case of rare genes. Thus, with fibrocystic disease of the pancreas, which occurs about once in 2000 births, the excess of cousin marriages among the parents is inappreciable. The second point is that the proportion of genes in common falls off rapidly as relationship becomes more remote. As already mentioned, the proportion is one-eighth for first cousins, but only one-thirty-second for second cousins, i.e. the offspring of first cousins, so that fairly remote blood relationship can reasonably be safely ignored.

J. A. FRASER ROBERTS, M.D., F.R.C.P.

PRACTICAL NOTES

Complications of Acute Nephritis

THE three serious, if uncommon, complications of acute nephritis in children are oliguria or anuria, electrolyte disturbance, and hypertensive encephalopathy. In reviewing the methods of dealing with these complications at the Mayo Clinic, E. C. Burke (*Proceedings of the Staff Meetings of the Mayo Clinic*, January 22, 1958, **33**, 23) recommends the use of surface area as the basis for calculation of fluid needs. Such a calculation ordinarily requires only a conversion from weight to surface area, for which tables are available. The water requirements can be met orally or intravenously—preferably orally. The Mayo Clinic workers do not subscribe to the older theory that 'intravenous water loading forces diuresis'. Should intravenous administration be considered necessary, a 10% solution of dextrose in water should be used in amounts varying from 400 ml. per square metre daily in older children to 1000 ml. per square metre daily in younger children and infants. At times it may contain 0.2% sodium chloride in an attempt to lower the concentration of serum potassium. The child should receive 50 to 75 g. of dextrose per square metre of body surface daily. Whether this be given as 'hard candies, in carbonated drinks, or in intravenous solutions' is for the physician to decide in the individual case. The major hazard of electrolyte disturbance is a rise in the serum potassium to a level which may prove dangerous to the heart. Promising results have been obtained in lowering the serum potassium concentration by the use of repeated enemas of carboxylic acid resin: 50 g. of resin per 500 ml. of water; 250 ml. of this suspension, with 4 tablespoons of methylcellulose liquid to effect a satisfactory suspension, were given every four hours. Hypertension can be controlled by a daily intramuscular injection of a combination of reserpine and hydrallazine, in a dose of 0.15 mg. of each per kg. of body weight when the blood pressure rises above 140 mm. Hg systolic and 100 mm. Hg diastolic.

Corn Oil in Coronary Disease

THE effect of corn oil has been investigated by L. Tobian and N. Tuna (*American Journal of Medical Sciences*, February 1958, **235**, 133) in 23 patients with coronary disease: 15% of them had had a previous myocardial infarction and 18% had angina pectoris. They were given 1 to 1½ ounces (28.5 to 42 ml.) of corn oil thrice daily, either undiluted or emulsified with flavoured water. In addition, they used corn oil as a cooking and salad oil. Five of the patients were given no other dietetic instructions; 18 were instructed to eat very little butter fat or hydrogenated vegetable fats. About one-quarter of the patients had 'slight indigestion' while taking 1½ ounces (42 ml.) of corn oil with each meal, but only one out of 25 had indigestion while taking 1 ounce (28.5 ml.), and he had a

duodenal ulcer. In 70% of cases there was at least a 15% decrease in serum cholesterol following the use of corn oil, in 26% the decrease ranged from 9% to 14%, and in only one patient was there no significant decrease. It is stated that 'the drop in cholesterol has been continuously maintained during a whole year of corn oil ingestion' and that 'none of these patients had any exacerbation of angina pectoris while taking corn oil'.

'Spansule' Phenobarbitone in Psychotic Epilepsy

'STRIKING improvement' in patients with psychotic epilepsy treated with 'spansules' of phenobarbitone instead of phenobarbitone in solution or tablet form is reported by D. C. J. O'Connor (*Lancet*, 1958, **i**, 609). At the beginning of a trial in a series of 18 psychotic epileptic male patients who had had convulsions and psychoses for more than ten years, nine were receiving an average daily dose of 168 mg. of phenobarbitone solution or tablets, four were receiving the phenobarbitone plus 0.25 to 1.25 g. of primidone, and five were on primidone alone. Eleven patients were also receiving occasional electroconvulsive therapy 'for fluctuation in mood'. With the intention of maintaining a constant blood content of phenobarbitone throughout the twenty-four hours, 'spansules' of phenobarbitone (which allow even absorption and steady blood levels) were gradually substituted for the solution or tablets, or added in those cases receiving primidone alone. The mean daily dose was 348 mg., and during the change-over patients were 'carefully assessed every day, and the dosage reduced if there was any sign of drowsiness, muscle incoordination, or impairment of balance'. During the year before the beginning of the change-over the group had a total of 799 convulsions, but by the end of the two years during which the change-over was made 'no patient was having convulsions in any form', although two did not start the new treatment until the beginning of the second year. In some of the more difficult cases up to five 'spansules' (480 mg.) were given daily without ill-effects. Improvement in personality was 'striking' in 12 cases, 'moderate' in 3, and 'slight' in 2. Only one patient failed to improve. Improvement in mental state was particularly noticeable in the nursing of the patients 'who became less noisy and aggressive and better behaved during the day, with gradual but complete elimination of all disturbance at night and a full night's sleep in each case'. All signs and symptoms of toxic effects were much improved. 'The good effects and low toxicity are attributed to the constancy of the blood-barbiturate level that was attained'.

Ice-Cube Anæsthesia

'CHILLING the skin with an ice cube of 1:1000 aqueous benzalkonium chloride ('zephiran') gives quick, painless, superficial anæsthesia plus antisepsis', according to M. C. Zimmerman (*A.M.A. Archives of Dermatology*, January 1958, **77**, 122). The cubes are made by diluting 4 ml. of stock aqueous 12.8% commercial concentrate of benzalkonium chloride with 500 ml. of water. This makes one tray (14 ice cubes) of 1:1000 benzalkonium chloride solution, costing $\frac{1}{5}$ cent per cube. An added drop or two of any dye (e.g. gentian violet, Parker 51 ink, methylene blue), it is said, 'provides a touch of "magic" for younger or older patients who ascribe anæsthetic potency to the colour'. It is primarily recommended for use preceding desiccation of superficial blemishes of the skin by means of the electrocautery, but is also useful in apprehensive children (or adults) preceding intravenous, subcutaneous or intradermal injections. The procedure recommended is that the nurse removes a cube from the tray, wraps one end in a paper towel and hands it to the patient who is asked to press it firmly against the skin at the required site for 15 to 30 seconds.

Infective Polyneuritis and Cats

EVIDENCE that at least a proportion of cases of so-called infective polyneuritis (the Landry-Guillain-Barré syndrome) may be due to a virus infection acquired from cats is adduced by A. M. G. Campbell (*Proceedings of the Royal Society of Medicine*, March 1958, **51**, 157). He has seen six cases in which the onset of the disease was directly related to an illness of the patient's cat, and he knows of five other cases in which the condition was linked with an illness in a cat. The most interesting of these cases was that in which a Dorset farm labourer developed infective polyneuritis. His cat was sent to a school teacher, aged 65, who lived forty miles away, to be looked after while he was ill. A month later the cat sickened and died of feline enteritis, and the school teacher was admitted to hospital with an acute infective polyneuritis. There are two main infectious diseases of cats. One is an influenza-like illness involving the lungs and due to a large virus of the psittacosis family. The other is feline enteritis, which is highly infectious among cats, affecting chiefly young cats and kittens, and it is estimated that at some time or other 70% of cats are infected. It is this latter which, it is contended, might be responsible for causing infective polyneuritis in man. Preliminary investigation with a complement-fixation reaction on the sera of patients, using as antigen cats' tissue infected with feline enteritis virus, suggests that there is a distinct

difference between the blood of patients with infective polyneuritis and that of controls.

Radioactive Chromic Phosphate in Malignant Effusions

THE use of radioactive colloidal chromic phosphate ($Cr\ P^{32}\ O_4$) is recommended by M. L. Jacobs (*Journal of the American Medical Association*, February 8, 1958, **166,** 597) for the treatment of malignant pleural and peritoneal effusions. Compared with radioactive gold, it is said to be much simpler to handle, safer and less expensive. He reports his findings in 41 cases of malignant pleural effusion, and 16 cases of malignant ascites. 'Good results' were obtained in 60.9% of the former, 11 of the patients having periods of freedom of six months or longer. Of the 16 patients with malignant ascites, 31.2% had 'good results'. The one serious consequence of such treatment is necrosis of the adjacent intestinal wall should loculation of the radioactive material occur, as it did in one patient in this series. It is often difficult to ascertain whether such areas of loculation exist, but, 'if, in the process of paracentesis, it is evident that there is loculation, this must be considered a contraindication to the instillation of radioactive material'.

Woltman's Sign

IN myxœdema the muscle stretch reflexes show a characteristically delayed relaxation after contraction. This is the basis of Woltman's sign of myxœdema (so-called after the distinguished American neurologist who first described it forty years ago) or the myxœdema reflex. It has been described as 'probably more specific for the diagnosis of myxœdema than the basal metabolic rate'. In reporting five cases in which he found it of value, C. S. Houston (*Canadian Medical Association Journal*, January 15, 1958, **78,** 108) describes the method of eliciting the reflex as follows. The patient is seated on the examination couch, with the legs dependent, the foot is held gently in one hand and the tendo Achillis tapped with the reflex hammer. The extent of the response may be diminished or normal. The crucial part is the relaxation phase: instead of quickly returning to the starting position, the foot comes back very slowly, taking almost a second to return. It is said that 'once one has felt the slow relaxation of a myxœdema reflex it is surprisingly easy to differentiate this from a normal reflex'. In advanced cases of myxœdema, of course, with absent or very sluggish reflexes, the sign is not elicited, but in these cases the diagnosis is obvious in any case. It is claimed that no 'false positives' have ever been recorded in the literature.

Hypervitaminosis A

YET another case of hypervitaminosis A has been reported. This time by T. K. Oliver, Jr. (*A.M.A. Journal of Diseases of Children*, January 1958, **95,** 57). The patient was a 14-year-old white girl who for ten months had been taking 200,000 units of vitamin A prescribed for the treatment of acne vulgaris. Two months before admission she noticed scaling and fissuring of her lips. This was followed by pains in the legs, falling out of the hair, and hypomenorrhœa, a maculopapular eruption and increasing irritability. On examination the major findings were fissuring of the lips, a diffuse papular eruption, marked desquamation of the soles of her feet, moderate alopecia, tenderness in both legs, bilateral papillœdema with linear hæmorrhages around each disc, and a cerebrospinal fluid pressure of 600 mm. H_2O (in the supine position). The patient was asymptomatic within a fortnight except for continued loss of hair. Regrowth of scalp hair did not begin until six weeks after the vitamin A was stopped. This is said to be the 36th case of hypervitaminosis recorded in the American and British literature since 1944. In this group x-ray evidence of bony changes was found in all the infants and toddlers but in only one of the nine children and adults. Neurological symptoms and signs due to increased intracranial pressure were present in 20% of cases. All symptoms and signs subsided completely following withdrawal of the vitamin.

Treatment of Filariasis

DIETHYLCARBAMAZINE is an 'effective drug' in the treatment of *Wuchereria* filariasis, according to a report published by WHO (*Chronicle of the World Health Organization*, December 1957, **11,** 365). It is administered orally, and the usual dosage schedule is 2 mg./kg. daily, three 10-day courses being given at intervals of two or three weeks. It acts by promoting phagocytosis of the filariæ by the macrophages. The massive destruction of the filariæ leads to secondary effects of an allergic nature, such as headache, articular pains and fever. These are partly relieved by acetylsalicylic acid or by antihistamines, 'but, nevertheless, constitute an obstacle to mass treatment'. It is also used, in a dose of 6 mg./kg. once a month for a year, for mass chemoprophylaxis—given to the entire population, including persons whose blood is free from microfilariæ. On this regime, in Tahiti the filarial rate fell from 30% to 3% in three years; more than half the positive cases were found in immigrants or people who had refused treatment. The annual cost of treatment was $3 per inhabitant. Individual treatment by mosquito netting in the home and the wearing of clothing out of doors should not be neglected.

REVIEWS OF BOOKS

Cancer. Vol. I, II. Edited by RONALD W. RAVEN, O.B.E., T.D., F.R.C.S. London: Butterworth & Co. (Publishers) Ltd., 1957. Pp. x and 558; ix and 666. Figures 94 and 357. Price 85*s.* per volume.

THE first volume of this encyclopædic review of cancer is devoted to 'research into causation' and the contributors are drawn equally from the two sides of the Atlantic. A curious omission from this volume is a chapter on the epidemiology of cancer—one of the most promising approaches to the problem at the present day. In future editions a chapter on this subject might well replace the somewhat negative one on 'the incubation of cancer in man' in the present edition. All the other important aspects of the subject, however, are adequately and competently covered, including 'the biochemistry of cancer induction'. 'hormones and neoplasms', 'the part played by viruses in the origin of tumours', and 'nutrition and the genesis of tumours'. The second, and larger, volume is devoted to the 'pathology of malignant tumours', and the contributors are drawn predominantly from the United Kingdom. These include such well-known names as R. A. Willis ('modes of spread of malignant tumours'), Cuthbert Dukes ('colon, rectum and anus'), Edith Dawson ('breast'), and Agnes Macgregor ('children').

This is a notable contribution to the subject and will prove invaluable to research workers and pathologists as a work of reference. In view of the rapid advances being achieved in this field it is obviously impossible for any book on the subject to be right up to date. What is most useful, however—and what this book achieves—is an authoritative review of the subject at one particular time which can act as a base-line of knowledge for future advances.

Hepatitis Frontiers. Edited by FRANK W. HARTMAN, M.D., *et al.* Boston: Little, Brown & Co., London: J. & A. Churchill Ltd., 1957. Pp. xvii and 595. Price £5 10*s.* Illustrated.

THIS book is an account of the proceedings of a meeting sponsored by the Henry Ford Hospital at Detroit and held there in October 1956. Seventy contributors took part in the project and the book includes not only their original papers but also verbatim accounts of the discussion which followed each group of papers and of special panel discussions on differential diagnosis and on therapy. The book is divided into six main sections. The first, which deals with the anatomy, physiology and pathology of the liver, has an excellent section on the histological changes in viral hepatitis which should be read in conjunction with an account later in the book of the results of needle biopsy of the liver. Two sections deal with prophylaxis and especially with the problem of the selection of blood donors and of methods for inactivating the virus in blood and blood products. The two last sections on differential diagnosis and clinical management are of special interest to the practising physician. The controversial problem of the place of cortisone in the treatment of infective hepatitis is fully discussed and there is a good account of the management of hepatic coma.

Inevitably there is much repetition in a book of this type and the panel discussions throw into sharp relief the differences of opinion shown by experts from different countries. One gains the general impression of vast activity in this field and it will not be the fault of these seventy enthusiasts if the present incidence of viral hepatitis and of its more serious complications continues unchecked.

Portal Hypertension. By ALAN HENDERSON HUNT, D.M., M.CH., F.R.C.S. Edinburgh: E. & S. Livingstone Ltd., 1958. Pp. xi and 230. Figures 120. Price 40*s.*

MANY fine monographs have had their professional debut as Jacksonian Essays or Hunterian Lectures. This book comprises the Jacksonian prize-winning essay for 1956 and, as the author writes from an experience of 250 unselected cases of the condition of which he has had personal experience, it must be regarded both as authoritative and as well summarizing the present state of our knowledge of portal obstruction and the procedures adopted for its relief. Various chapters deal with the anatomy of the portal vein and related structures: the causes, types and effects of its obstruction, the indications for operative treatment and the results which may be expected from it. In a series of appendices, technical considerations are dealt with, such as splenic venography, the types of portal systemic anastomosis and ligature of œsophageal varices and a final section consists of a series of selected and summarized case histories. There is an extensive bibliography. The format of the book is attractive as it is printed in large clear type and well illustrated throughout.

In his advocacy of either porto-caval or lienorenal anastomosis to decompress the portal system, the author is an enthusiast, claiming that after deprivation of its portal blood supply or even occasionally after hepatic ligature the liver can sometimes improve in function. The results of these shunt operations are variable,

some patients improving while others deteriorate, and so far it has not been possible to determine before operation which will give favourable results. The author is to be congratulated on an important contribution in which all who are interested in the problem of portal obstruction will find much to help them.

Office Gastroenterology. By Albert F. R. Andresen, M.D. Philadelphia and London: W. B. Saunders Co., 1958. Pp. xxxiv and 707. Figures 110. Price 98*s*.

Dr. Andresen's 40 years' experience in teaching and practice is incorporated in this monograph, which is designed to be a practical book presenting simple specific information about the diseases of the alimentary tract (excluding the mouth) and their treatment by general practitioners. The book is arranged in five sections: (1) a general outline of symptoms, history and examination and the physiological basis of treatment, (2) diseases affecting the entire tract, (3) disease of the various parts of the tract, which is the largest section, (4) the liver and biliary tract, and (5) general disease with manifestations in the gastro-intestinal tract. This arrangement leads to much duplication (though cross-references are available in the text) and to vague unhelpful statements which are far from practical. Dr. Andresen's predilection for allergic disease is well known. The chapter on gastro-intestinal allergy comprises 20 pages, that on psychosomatic disorders 3 pages. Few will go so far with him as to say (page 367) 'Both the large and small intestines are frequently the site of allergic reactions'.

The book is well produced: the illustrations, particularly the x-ray reproductions, are well chosen. Careful editing and rearrangement might well have reduced the length of the text and made space available for a bibliography which in spite of Dr. Andresen's argument is essential to a worth-while text. He is not sufficiently orthodox a writer to be able to dispense with references to his sources.

Gastro-Intestinal Obstruction. By Meyer O. Cantor, M.D., and Roland P. Reynolds, M.D., *et al*. Baltimore: Williams & Wilkins Co.; London: Baillière, Tindall & Cox Ltd., 1957. Pp. xii and 565. Figures 415. Price £7 4*s*.

This book is a complete survey of the whole problem of obstruction of the human alimentary tract. It is well written and well illustrated, and it leaves nothing out. The only possible comment is that of L. Cassius, an upright statesman of ancient Rome, who always inquired of any proposal that was made, however popular, 'cui bono fuisset'—who would benefit by it. The only people who want a book that tells 'all about everything', that leaves no literature unexplored and no authority unquoted, are the librarians and research workers. Students want to know a lot about a subject, but they want the information selected and explained for them. Surgeons want a monograph on certain aspects of a subject, but they do not want to go back to the beginning. This book is really a monograph on the 'Cantor Tube', undoubtedly the best of the many gadgets designed for intestinal decompression. Chapter 18 on gastro-intestinal intubation and Chapter 19 on water and electrolyte balance, are the parts that the average surgeon would want to read. The Cantor tube keeps recurring in each chapter like the Siegfried motif in 'The Ring'.

Cerebral Palsy in Childhood. By Grace E. Woods, M.D., D.P.H., D.C.H. Bristol: John Wright & Sons Ltd., 1957. Pp. xi and 158. Figures 41. Price 27*s*. 6*d*.

This book is the result of a clinical study of 301 cases referred to the Cerebral Palsy Assessment Clinic of the Bristol Royal Hospital for Sick Children. The cases are classified clinically into seven groups descriptive of the '. . . upset of movement pattern . . .': paraplegia, monoplegia, hemiplegia, quadriplegia, athetosis, ataxia and rigidity. On the grounds of the retrospective study of the clinical histories, an attempt is made to assess the relative importance of various etiological factors. It is thus apparent that all the clinical groups are etiologically heterogeneous. Omitting the definitely familial and hereditary cases, cases with known congenital defects and cases of postnatal origin, Dr. Woods concludes that 'the over-all evidence is that . . . the significance of an abnormal birth history is very marked'. In what is in effect the second part of her book, the author passes on to consider the other handicaps of children with 'cerebral palsy', such as the visual defects, the auditory and speech defects, the sensory defects including those that are called, in adults, parietal lobe syndromes, the convulsive handicap, and the intellectual handicap considered under the broader heading of 'assessment of educability'.

Dr. Woods's findings are generally in keeping with those of other workers in this field, but interesting points are raised and novel viewpoints disclosed and suggestions made. The author was well served by a team consisting of an educational psychologist, teachers, and therapists. The book will be of interest to all who have knowledge of this subject and who deal with the various clinical, educational and therapeutic or remedial problems of the child affected by 'cerebral palsy'.

An Introduction to Electrocardiography. By L. SCHAMROTH, M.B., M.R.C.P.ED., F.R.F.P.S. Oxford: Blackwell Scientific Publications, 1957. Pp. xi and 60. Figures 106. Price 12*s.* 6*d.*

ELECTROCARDIOGRAPHY is now much less empirical than formerly and some basic knowledge of the principles concerned is essential for all who have the responsibility of interpreting electrocardiograms and of interest to all who wish to understand and remember. The information in this small volume will be found in textbooks but in none is the material so clearly expressed, explained and illustrated. The text is profusely interspersed with simple diagrams and figures. It forms an excellent introduction to the subject and will be of value to undergraduates, postgraduates and physicians who have previously found the matter too complex. Sixpence a page is not too much to pay for such instruction.

Ideals in Medicine. Edited by VINCENT EDMUNDS, M.D., M.R.C.P., and C. GORDON SCORER, M.B.E., M.D., F.R.C.S. London: The Tyndale Press, 1958. Pp. 192. Price 12*s.* 6*d.*

THE production of this book fulfils a useful purpose. The aim of the various contributors has been to establish a code of Christian ideals in medical practice. The approach is from many angles and a complete picture of the problems envisaged is presented. Sound general principles are stressed early in the book and these are more fully elaborated in subsequent chapters. The discourse on the 'distinctive ethical code' is illuminating and includes a comparison of 'medical ethics' and 'medical etiquette'. The section relating to ' The doctor's personal standards' contains sound and valuable advice, whilst the chapters entitled 'The satisfactions of a family doctor ' and ' The doctor's relationships' embody a high standard of medical ethics. 'The Christian approach to the disabled', the 'incurable' and the 'dying' is a most helpful contribution. The chapter entitled 'Some problems of psychological medicine' seems redundant. The controversial subject of 'Faith-healing' is thoughtfully and critically discussed. Medical missions are considered in some detail, and the chapter entitled 'The doctor himself' deals with the Christian standard of life.

The purpose of this book has been abundantly fulfilled by the general principles set forth for the guidance of the Christian doctor. These principles are tabulated under the heading 'Code of medical ethics' in an appendix. The contributors are to be congratulated on the clear, concise and helpful presentation of their subject. A comprehensive bibliography is included.

Memoirs of a Golden Age. By MAURICE DAVIDSON, D.M., F.R.C.P. Oxford: Basil Blackwell, 1958. Pp. xiii and 140. Illustrations 29. Price 18*s.*

SELDOM has Dr. Maurice Davidson's pen been put to better use than in this delightful evocation of an Oxford which is now rapidly fading into the mists of history. Those were the days when a university was still a university and not a glorified technical college, when dons were still allowed to be individualists, and undergraduates were taught and not dragooned. The myth of 'progress' has wrought havoc with the two ancient universities, and the country is the poorer for it. The red-brick universities have won the day and the glories that were Oxford's and Cambridge's are now a thing of the past.

If, alas, they cannot be revived, they can at least be recorded by those who were fortunate enough to share them so that future generations may know what they were. This is what Dr. Davidson has done. He was an undergraduate during the first four years of the century, but he throws his net much wider and recalls the great names that were already traditional in his day as well as those of his own generation. It is a book which will be read with fascinated interest by all Oxford men of the older generation and, as in the case of the reviewer, by many who, though not Oxford men, appreciate the great contribution that this ancient university has made to the cultural welfare of the nation.

NEW EDITIONS

Clinical Heart Disease, by Samuel A. Levine, M.D., F.A.C.P., in its fifth edition (W. B. Saunders Co. 66*s.* 6*d.*) has increased in size by 20% and in price by over 50%. In spite of both these adverse—and, unfortunately, not unique—features, it remains good value for money. Its aim has always been to appeal to the general practitioner, with its insistence upon the practical clinical aspects of the subject. It is Harvard at its best—clear, well written and judicial. The author seldom forgets that the chief function of the clinician—whether in general or consulting practice—is to help his patient, and that what is practicable is not always synonymous with a perfect diagnosis according to the standards of the clinical scientist. This is a book which the practitioner will find of continuing interest and value in his work.

Antisera, Toxoids, Vaccines and Tuberculins in Prophylaxis and Treatment, by H. J. Parish, M.D., F.R.C.P.ED., D.P.H., in its fourth edition (E. & S. Livingstone Ltd., 30*s.*), has undergone

radical revision in order to keep pace with the rapid changes in this increasingly important branch of medicine. There are, for instance, now five chapters devoted to immunization against virus diseases, compared with only two in previous editions. There is no book quite like this in the English language. It provides the clinician with a clear, concise, authoritative, and up-to-date review of what he needs to know on the subject. Any practitioner who omits to possess a copy of it is not only doing himself a disservice, he is depriving his patients of the full benefit of the great and various advantages bestowed upon the community by modern methods of immunization. This is one of the very few 'musts' in medical literature.

Recent Advances in Oto-laryngology, by F. Boyes Korkis, M.B., F.R.C.S., D.L.O., in its third edition (J. & A. Churchill Ltd., price 60*s*.) is for all practical purposes a new book. As Mr. R. Scott Stevenson, the author of the first two editions, points out, 'advances in oto-laryngology have been so many in recent years, and the literature of the specialty has been so voluminous, that the subjects selected for appraisal and discussion in the present book bear little resemblance to those discussed in the previous editions'. To change horses in midstream is always difficult and sometimes hazardous. In this instance the operation has been entirely successful. The new edition retains all the admirable characteristics of its predecessors and will continue to fill a gap in the literature of the subject, providing the otolaryngologist with a concise, authoritative, and up-to-date assessment of the important advances in the specialty during the last decade.

Child Psychiatry, by Leo Kanner, M.D. (Blackwell Scientific Publications, 63*s*.).—This well-established textbook is greatly enlarged in its third edition. The little known Meyerian terminology has been discarded, but the material is still arranged in a description centred on the symptom. Thus, encopresis is presented as a psychosomatic disorder of the digestive system, although the description given to it links it with anxiety and neurotic conflict. This tendency to break the text up into a multiplicity of descriptive labels may seem to diminish its value for the experienced worker. Ample recompense is made, however, by a comprehensive bibliography (European as well as American), attached to every section. Each subject can thus be studied more fully than is possible in so comprehensive a textbook. The section on therapy has been completely rewritten, and to great advantage, but the space given to treatment is still disappointingly small, and little is said of residential treatment of disturbed children. Nevertheless, this remains a valuable textbook, reflecting its author's encyclopædic knowledge of his subject, and outstandingly generous in acknowledgement of the work of others in the same field.

A Text-book of X-ray Diagnosis, Vol. I, edited by S. Cochrane Shanks, M.D., F.R.C.P., F.F.R., and Peter Kerley, C.V.O., C.B.E., M.D., F.R.C.P., F.F.R., D.M.R.E., third edition (H. K. Lewis & Co. Ltd., 90*s*.).—The first volume of the four which make up this deservedly popular textbook to appear in this edition deals with the radiology of the head and neck and the central nervous system. The authors have resisted the temptation to make drastic changes and the work remains a sound exposition of British radiological practice in these fields. At the same time the contributors have fully acknowledged the debt which neuro-radiology owes to the Scandinavian workers. Little major change has taken place in the last few years in the practice of ventriculography and encephalography, but further data have enabled us to assess more accurately their value and that of cerebral angiography in the investigation of intra-cranial expanding lesions. The various lesions which can be demonstrated by these contrast methods are copiously illustrated by radiographs and line drawings and the underlying principles are clearly explained. The relatively short section on myelography is in keeping with the modern tendency to find fewer indications for this technique. The bibliography is selective and includes all the classical papers on neuro-radiology but is perhaps a little deficient in recent references.

The short chapter on the eye concentrates chiefly on the modern simpler methods of foreign-body localization whilst that on the accessory nasal sinuses and temporal bone concerns itself entirely with inflammatory conditions to the exclusion of some interesting neoplasms. As in the previous editions, part II on 'The Teeth and Jaws' by H. M. Worth is quite outstanding. Clearly printed and well written, this work will continue to be a valuable source of information to radiologists and clinicians and it is the essential book of reference for those intending migrants whose future practice is likely to embrace some radiology, however little.

The contents of the June issue, which will contain a symposium on 'Midwifery,' will be found on page A126 at the end of the advertisement section.

Notes and Preparations see page 639
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NOTES AND PREPARATIONS

NEW PREPARATIONS

'ALUDROX' CO tablets each contain 420 mg. of dried aluminium hydroxide and 65 mg. of light magnesium carbonate 'with patient-tested flavouring and saliva-stimulating agents', and are intended for the treatment of peptic ulcer. When allowed to dissolve slowly in the mouth they 'release a steady stream of antacid juice to the stomach thus ensuring continuous neutralizing of excess free acid between meals'. Issued in boxes of 48 tablets packed in cellophane strips of eight. (John Wyeth & Brother Ltd., Clifton House, Euston Road, London, N.W.1.)

'CORLAN' pellets each contain 2.5 mg. of hydrocortisone hemisuccinate sodium and are intended primarily for the treatment of simple aphthous ulceration of the mouth and as adjuvant therapy when aphthous ulceration complicates conditions such as sprue. The pellets should be allowed to dissolve in the mouth in close proximity to the ulcer. Issued in tubes of 20 tablets. (Glaxo Laboratories Ltd., Greenford, Middlesex.)

'DISTAVAL' tablets (scored) contain thalidomide, a new sedative and hypnotic 'free from barbiturates, bromine compounds and alkaloids'. They are said to produce 'a smooth, calming effect without producing either euphoria or an initial phase of excitement', to induce rapid and profound sleep and to be free from side-effects. Available in strengths of 25 mg. (in tubes of 24 and bottles of 100 and 500) and 100 mg. ('distaval' forte, in tubes of 12 and bottles of 100). (The Distillers Co. (Biochemicals) Ltd., Broadway House, The Broadway, Wimbledon, London, S.W.19.)

'LEDERCORT' tablets each contain 4 mg. of triamcinolone, which is a new synthetic steroid 'with enhanced glucocorticoid and markedly diminished mineralocorticoid characteristics'. Among the advantages claimed for this drug are that in general the dosage required is only two-thirds that of prednisone or prednisolone; that instead of causing water and sodium retention 'it either exerts no effect, or actually produces sodium diuresis'; that there is no interference with psychic equilibrium and appetite is rarely disturbed. Issued in bottles of 30 and 100 scored tablets. (Lederle Laboratories Division, Cyanamid of Great Britain Ltd., Bush House, Aldwych, London, W.C.2.)

'LOREXANE' no. 3 ointment contains 2% gamma benzene hexachloride B.P. in 'a harmless detergent base' and is intended especially for the family treatment of head lice. Available in tubes of 50 g., which is sufficient for eight treatments. (Imperial Chemical Industries Ltd., Pharmaceuticals Division, Fulshaw Hall, Wilmslow, Cheshire.)

'VASCUTONEX' cream contains 10% glycol salicylate and 10% diethylamine salicylate and is indicated in 'conditions of acute and chronic extra-articular and articular rheumatism, periarthritis of the shoulder and osteoarthritis'. It is stated that it has prolonged action, is non-staining, odourless and contains no counter-irritants. Issued in tubes containing 30 g. (Calmic Ltd., Crewe, Cheshire.)

PHARMACEUTICAL NOTES

AMES CO. (LONDON) LTD. announce the introduction of 'albustix' reagent strips for urine protein, with which 'even cloudy urine can be tested without filtration' in a few seconds (supplied in bottles of 60 sticks); and 'hematest' reagent tablets which provide a standardized *o*-tolidine test for occult blood in the fæces. This latter test has the same sensitivity as the Gregerson test but avoids the use of benzidine. Supplied in bottles of 50 tablets. (Nuffield House, Piccadilly, London, W.1.)

ROUSSEL LABORATORIES LTD. announce that 'hydrocortisyl' skin lotion is now available in an additional lower strength of 0.25%. Supplied in plastic bottles containing 20 ml. (847 Harrow Road, London, N.W.10.)

TRUFOOD LTD. announce that most of their 'spoonfoods' range of strained babyfoods are now being supplied in glass jars with a new vapour vacuum cap. This can be simply prized or levered off without damage to the cap which, when replaced, re-seals the jar. A metal 'flipper' for removal of the cap is supplied free with the product. (Green Bank, London, E.1.)

FILM NEWS

Breast Feeding (16 mm., colour, sound; running time 23 minutes) is a teaching film which was made at the British Hospital for Mothers and Babies at Woolwich as a tribute to the memory of Dr. Harold K. Waller. It is intended for nurses, midwives, mothers attending antenatal and postnatal clinics, and women's institutes. For sale at £45 per copy; hiring arrangements not yet announced. Available for private view by appointment with Stanley Schofield Productions Ltd., 6-8 Old Bond Street, London, W.1.

An Introduction to the Study of Child Health (16 mm., colour, sound; running time 20 minutes) is intended for university students, second-year medical students and nursing colleges, and shows the training of students in maternity and children's hospitals. Available for private view by appointment with Stanley Schofield Productions Ltd., and sponsored and distributed by Cow & Gate Ltd., Guildford, Surrey.

FORTHCOMING CONFERENCE

The Science and Art of Health Education will be the theme for this year's summer school organized by the Central Council for Health Education, to be held at Bishop Otter College, Chichester, from August 19 to 29, 1958. Full details may be obtained from the Medical Director, Central Council for Health Education, Tavistock House North, Tavistock Square, London, W.C.1.

HUNTERIAN SOCIETY'S GOLD MEDAL ESSAY COMPETITION

THE subject for the Hunterian Society's gold medal essay competition for 1958 is 'Impotence'. The competition is open to all general practitioners and further details may be obtained from the honorary secretary, Dr. C. W. Kesson, 51 Harley Street, London, W.1.

NEW JOURNAL

District Nursing is the new official journal of the Queen's Institute of District Nursing, replacing the *Queen's Nurses' Magazine*. Its aim is 'to serve all engaged in domiciliary nursing and allied medical, nursing and welfare services, and to help weld these into an integral whole'. The journal will be published monthly, price 1*s.* per copy, or 12*s.* per annum post free. (57 Lower Belgrave Street, London, S.W.1.)

R.A.M.C. DIAMOND JUBILEE

IN honour of the Diamond Jubilee of the Royal Army Medical Corps, a commemorative oration will be delivered in the Great Hall, B.M.A. House, Tavistock Square, London, W.C.1, on Wednesday, June 25, 1958, at 5 p.m. by Sir Gordon Gordon-Taylor, K.B.E., C.B., F.R.C.S. The title of his address will be 'In Arduis Fidelis'. The Band of the R.A.M.C. will play a selection of music in the Courtyard of B.M.A. House before and after the oration. Tickets will not be required.

NEW PHARMACEUTICAL PLANT

YET another American pharmaceutical company has built its own factory in Great Britain. The new plant inaugurated on April 15 by Cyanamid of Great Britain Ltd. for their Lederle Laboratories Division occupies a sixteen-acre site at Gosport, Hants, and employs nearly 300 people. This replaces the company's factory at Hirwuan, South Wales.

INFECTIVITY OF POLIOMYELITIS

'IT seems clear that in any household in which one member develops poliomyelitis a considerable proportion of the other members are infected too; in children under 5 years of age this proportion probably approaches 100%. Whatever therefore may be said for segregating these children, there is practically nothing to be said for protecting them with gamma globulin . . . By the time the primary case is diagnosed infection has already been disseminated throughout the household, and the taking of prophylactic measures such as the injection of gamma globulin is superfluous'. These are the major conclusions in a report of The Public Health Laboratory Service (*Monthly Bull. Minist. Hlth Lab. Serv.*, 1958, **17**, 58), based upon an investigation of 96 cases of poliomyelitis and 290 home contacts.

It is also noted that much the same proportion of children were excreting the virus during the 3rd and 4th as during the 1st and 2nd weeks after the onset of illness in the paralytic case. On this observation the authors of the report comment: 'We have no wish to use these figures in support of a longer period of quarantine—rather the reverse—but we do want to point out that the 3-week period is an arbitrary figure based largely on the practicability of enforcement, and affords little assurance that the contacts are likely to be much less infectious at the end than at the beginning of the period'.

TUBERCULOSIS AND CANCER

ACCORDING to provisional figures issued by the Registrar General for 1957, in England and Wales there were 4,250 deaths from respiratory tuberculosis, compared with 4,853 in 1956. This gives a death rate of 95 per million persons, which is a decrease of just over 12% compared with 1956, and means that since 1947 the death rate from respiratory tuberculosis has fallen by more than 79%. The provisional death rate for all forms of cancer was 2,312 per million population for men, and 1,890 for women. The comparable figures for 1956 were 2,274 for men and 1,891 for women. The rate for cancer of the lung and bronchus for men increased from 726 per million population in 1956 to 729 in 1957; the comparable increase for women was 111 to 116 per million. The provisional maternal mortality rate (including abortions) was 0.47 per 1000 live and still births—the lowest ever recorded. The previous lowest rate was 0.56 in 1956.

THE CONQUEST OF MALARIA

A SURVEY of 99 countries and territories just completed by the WHO shows that eradication of malaria has been achieved by nine countries (with a population of 231 million), including the United States of America, Puerto Rico, Chile, Cyprus, Corsica and Italy. In Southern Europe, where there used to be 4 million new cases of malaria annually, there are now less than 10,000. Ten years ago, malaria affected 300 million people a year and caused 3 million deaths annually. These figures have now been reduced by 50%. It is estimated, however, that in a country such as India the total loss of wage-earning capacity attributable to malaria is still in the region of $500 million a year.

SKIERS' HEARTS

CONFIRMATION that champion skiers have enlarged hearts is provided by M. J. Karvonen *et al.* (*Ann. Med. intern. Fenn.*, 1957, **46**, 169) as a result of a radiological study of 56 champion male skiers and 15 female skiers. On the other hand, there is no evidence that the hearts of skiers are any larger than those participating in other endurance sports such as long distance running. That enlargement of the heart during training has no serious consequences is suggested by the fact that the mean expectation of life of Finnish champion skiers exceeds that of the general male population by seven years.

PROCAINE BLOCK FOR NOCTURNAL ENURESIS

OF 40 cases of nocturnal enuresis treated by means of procaine block, 29 were cured and 11 much improved, according to a report in the *Chinese Journal of Pediatrics* (1957, **8**, 454). The procedure was to inject 10 to 50 ml. of procaine (0.5% to 2%) intradermally in the lower abdomen, so as to produce weals of about 2 cm. in diameter, 0.5 cm. apart. The injections were made along the linea alba between the umbilicus and the pubis, and then along the upper margin of the os pubis.

APPENDICITIS IN A CENTENARIAN

A SUCCESSFUL operation for gangrenous appendicitis in a lady aged 100 years and four months is reported by a correspondent in the *Medical Journal of Australia* (1958, **i**, 90). She made an uninterrupted recovery and was discharged from hospital on the tenth day.

THE MIGRANT SCOT

THE Scots are still on the move. According to a statement issued from St. Andrew's House, Edinburgh, the net migration from Scotland in 1957 was 35,500 compared with 24,600 in 1956. Although 10,800 of these migrants went to other parts of the United Kingdom, mainly England, Sassenachs will be relieved to learn that the movement to England was 700 down compared with 1956. The most interesting feature of these emigration figures is the tremendous increase in emigration to Canada—20,000 compared with 8000 in 1956.

ANTIBIOTICS AND WHALES

OXYTETRACYCLINE is proving of value to the whaling industry in the preservation of whale carcases, according to a report in the *Pharmaceutical Journal* (1958, **180**, 219). The antibiotic is injected at the time of harpooning or just after. One Norwegian whaling company has reported that 90% of the oil obtained from whales treated in this way could be classified as first grade, compared with 65% in the previous season when no antibiotic was used.

U.S. MEDICAL FEES

IN the United States of America, in the last twenty years hospital costs have risen sharply, in contrast to doctor's fees. A report in the *Monthly Labor Review* shows that between 1936 and 1956 hospital room rates rose by 264.8%, dentists' fees by 82.1%, general practitioners' fees by 72.8%, and surgeons' fees by 59.5%.

HOUSEWIVES' CHOICE?

A LIQUID cleaner for rugs and upholstery, which is about to be marketed in the United States, contains a new additive which, according to the *Financial Times*, is said 'to be capable of destroying all known disease-producing germs on contact', and to be 'self-deodorizing, mildew static, fungistatic and mould static'. This effect persists for three months following one application.

AMERICAN ALCOHOLISM

THE number of alcoholics in the United States has risen from one million to five million during the last five years, according to the executive director of the National Council on Alcoholism.

PUBLICATIONS

The Medical Directory 1958.—The 114th annual issue, contains 89,468 names—over 2000 more than the previous issue. As integral a part of the medical profession as any official publication—and much more useful than many of the latter—this product of private enterprise maintains its high standards of accuracy, comprehensiveness, and convenience of reference. This last attribute might be enhanced if an extra 'local list' could be incorporated, listing practitioners abroad according to their country. (J. & A. Churchill Ltd., price 84s.)

Current Therapy 1958, edited by Howard F. Conn, M.D., the tenth in the series, runs true to form as a reliable and up-to-date guide to therapy. No new form of treatment is introduced simply because of its novelty. Throughout, the aim is to concentrate on those newer remedies which can safely be used by the practitioner. On the whole an admirable balance is maintained and a commendable degree of caution displayed in recommending the latest additions to the practitioners' therapeutic armamentarium. (W. B. Saunders Co., price 84*s*.)

Why Stammer, by H. St. John Rumsey, M.A.—Mr. Rumsey wrote his first book on stammering in 1922, a year before he became the first speech therapist at Guy's Hospital. He uses his wide knowledge of speech in general, singing and elocution to aid the stammerer. He believes in tackling children early, and in a direct attack on the stammer. Psychological considerations are thought to be of secondary importance, at least in the beginning. His pupils are re-educated by being made to sing, speak more slowly and on a lower note, while continuous practice is the watchword. The author's learning and enthusiasm make the book pleasant as well as helpful reading for the student or sufferer. (Faber & Faber Ltd., price 8*s*. 6*d*.)

Medical Teleology and Miscellaneous Subjects, by F. Parkes Weber, M.D., F.R.C.P.—A member of a group discussing an obscure problem recently interjected with the comment that he had spent a long time looking through the writings of Dr. Parkes Weber and had found no comparable case. The effect this had on the discussion made it clear how much his works are valued, and thus how warm a welcome will be given to his latest volume. This contains not only fragments from his experience, but references to his past publications and comments on the more important recent ones of others. We thus know what he thinks about some problems in the light of recent information—and what a range he has! (H. K. Lewis & Co. Ltd., price 15*s*.)

The Patient Speaks, by Harold A. Abramson, M.D.—These glimpses into selected disclosures in the successful psychoanalysis of an allergic woman leave the reader in no doubt about the therapeutic skill of Dr. Abramson. What the patient says about her mother is sound evidence of a deeply disturbed mother-child relationship. The psychoanalytical interpretations of her illness are much more slenderly based. One cannot discount the influence of the prior expectations of the author on the content of the analysis. The sceptic will remain unconvinced but the book is confidently recommended to doctors and others interested in psychotherapy. (Vantage Press Inc., price $3.50.)

National Register of Medical Auxiliaries.—Registers of Audiology Technicians and Technicians in Venereology have now been published. Copies will be supplied free to members of the medical profession on application to the Registrar, Board of Registration of Medical Auxiliaries, B.M.A. House, Tavistock Square, London, W.C.1.

The General Nursing Council of England and Wales: Its History and Functions, by M. Henry, S.R.N., is reprinted from articles which appeared in the *Nursing Mirror* in January 1958. (Nursing Mirror, Dorset House, Stamford Street, London, S.E.1, price 1*s*. 9*d*. post free.)

What your Heart Does and *Heart Disease in Pregnancy* are the first of a series of leaflets on cardiac conditions to be issued by the NAPT Cardiac Information Centre. They are written in simple, non-technical language 'to help the cardiac patient, the family, and those responsible for their care'. (National Association for the Prevention of Tuberculosis, price 12*s*. 6*d*., and 10*s*. a 100 copies respectively, or 2*d*. each.)

Kleine Orthopädie, by Dr. Med. Gerhard Exner.—Although designed as an intruductory textbook for students this would be excellent as a quick reference work for busy general practitioners who wish to revise particular problems in orthopædics. A preliminary section upon methods of investigation and treatment is followed by one upon general disorders of the locomotor apparatus and a final section upon regional orthopædics. Each entity is given a clear, concise and accurate description. Treatment is briefly mentioned, and prognosis indicated. The illustrations are good. There is no discussion of acute injuries and fractures, and very little about the surgery of the hand. (Georg Thieme, price DM 9.80.)

International Sanitary Regulations is an annotated edition of the Regulations adopted by the Fourth World Health Assembly in 1951 and amended by the Eighth and Ninth Assemblies in 1955 and 1956. (H.M. Stationery Office, price 5*s*.)

The Planning of International Meetings is a handbook issued by the Council for International Organizations of Medical Sciences. It will be read with profit by those who have to organize such meetings, and with interest by those who attend them. (Blackwell Scientific Publications, price 7*s*. 6*d*.)

NOTES FROM THE CONTINENT

A European Newsletter

BELGIUM

Poliomyelitis.—Much thought has been given to the problem of poliomyelitis vaccination. In 1956 the incidence of poliomyelitis among children aged 1 to 5 years was twice that among those aged 6 to 10 years, whilst the incidence among the latter was three times that among adolescents aged 11 to 15 years. An investigation of over 7000 subjects drawn from all parts of the country showed that, of those aged 4 years over 23% had antibodies to all three types of poliomyelitis virus and that 75% had antibodies to at least one type of virus. Amongst army recruits, aged 20 years, 47% had antibodies against all three types. On the other hand, only 23% of students entering the university, whose ages ranged around 20, had complete immunity, whilst of 14-year-old children of doctors, engineers, and lawyers, only 11% had antibodies against all three types of virus. Of the 1,028 cases in the 1956 epidemic, 45% were aged 4 years or under, 72% were aged 9 years or under, and 87% were aged 19 years or under. The incidence of the disease was much heavier among those with no immunity than among those with potential immunity. In other words, the risk of developing the disease is highest on first encountering the virus.

In view of these considerations, it is recommended that all children aged 5 years or less should be vaccinated, as well as older children in the upper social classes. In the case of all other children their antibody status should first be ascertained, and immunization be dependent upon the findings. It is also recommended that, in view of the greatly increased risk of acquiring the disease, all adults going to the Belgian Congo should be vaccinated.

Orthopædics.—At a symposium on the management of bone and joint tuberculosis, conservatism seemed to be the predominant note. Sorrel did not consider the results of direct surgical attack on the lesion superior to ankylosing procedures, whilst Kastert reported an incidence of 40% of complications in a series of 1,100 cases of spinal tuberculosis treated by direct surgical attack. Gérard-Marchant reserves direct surgical attack for those cases of large Pott's abscesses not responding to rest and chemotherapy, but Debeyre reported excellent results from direct surgical attack followed by the local instillation of antibiotics.

Cardiology.—At a meeting of the Belgian Society of Biology, La Barre and Castiau reported that in dogs extracts of *Rauwolfia vomitoria*, which contain no reserpine, produced the hypotensive and tranquillizing effects of the latter without any gastric disturbance. In a dose of 1 mg. per kg. body weight, extracts of *Rauwolfia vomitoria* produced tranquillizing effects comparable with those of reserpine. They suggest that this means that such extracts may be of value in psychiatric cases in which full doses of reserpine often require to be given over long periods of time.

A new and, it is claimed, more accurate method of measuring cardiac volume has been put forward by Nylin. By means of two radiographs of the heart, taken at different angles, and a given mathematical formula cardiac volume is related to body surface. According to Nylin the upper normal limit is 500 ml. per square metre for men and 450 ml. per square metre for women. The two practical advantages claimed for this new method are that it allows easy and satisfactory control of the response to treatment in cases of heart failure, and the early detection of the onset of failure. A further development in vectorcardiography has been promulgated by Rijlant which is claimed to give more accurate information than either traditional limb or chest leads. In this new method, vertical, transverse, and antero-posterior records are obtained. A comparison with the results obtained by limb and chest leads is said to show considerable discrepancies.

Aortography is now a safe and standard procedure for investigation of many renal conditions, including the localization and extent of tuberculous disease, polycystic disease and suspected hypernephroma, according to Masy and his colleagues. In a series of 150 cases they have encountered only one serious complication.

Afibrinogenæmia.—In a paper read before the Belgian Society of Tropical Medicine, Lambillon and his colleagues gave details of 27 cases of afibrinogenæmia which they have seen in natives in Leopoldville since 1955. They stress that this condition is not only encountered in post-partum women, but can also occur following abortions and following gynæcological operations. A relapse is often as dangerous as the original illness. In treatment, plasma and preserved blood are of little value, unless the former is given quickly and in concentrated form. The treatment of choice is the administration of 2 to 6 grammes of fibrinogen.

Miscellanea.—François and Rabaey have described a method of micro-electrophoresis whereby the protein of aqueous humour can be estimated in amounts as small as 25 to 80

microlitres. By this method they report that in man the aqueous humour contains more albumen and less gamma globulin than serum, but approximately the same concentration of beta-globulin.

In these days of a rising mortality rate among medical journals, it is particularly fitting that note should be taken of one that has just celebrated its jubilee with a sumptuous jubilee issue—the *Journal Belge de Radiologie*.

FRANCE

Chemotherapy of malignant disease.—Ravina and Pestel have reviewed their results with cytostatic agents in the treatment of malignant disease over a period of four years. In spite of the occasional muco-cutaneous reactions which they sometimes produce, the most satisfactory responses have been obtained with actinomycin C and D. The best results have been obtained in chronic lymphatic leukæmia and Hodgkin's disease. Less satisfactory results have been obtained with thio-coleiran (R.261) and azan, although the former has proved promising in the treatment of certain superficial growths. On the whole the most promising results have been obtained with imine-quinone derivatives. Unfortunately their toxic effects severely limit their use, but the hope is expressed that in time a derivative of this group will be obtained in which the leucopoietic action sufficiently outweighs the toxic effects to justify its use in practice. In a series of 100 patients with malignant growths of various forms, treatment with E-39 (diethylene-2-3 dipropryloxy-3-benzoquinone), temporary improvement occurred in 37. In seven this was 'very marked', in 19 it was 'appreciable', whilst in 11 it was partial and of very temporary duration.

Primary carcinoma of the liver.—The high incidence of alcoholic cirrhosis of the liver undoubtedly explains the relatively high incidence of primary carcinoma of the liver in France, according to Benhamou and Fauvert, who have just reported their findings in 25 cases which they have encountered between 1947 and 1956 among 25,600 patients seen in three Paris clinics. There were 22 men and three women in this series, and confirmation of the diagnosis was obtained in every case—by either necropsy (22 cases) or biopsy (three cases). The diagnosis was hepatoma in 23 cases, and cholangioma in two. Analysis of post-mortem records showed that primary carcinoma of the liver occurred in 2.36% of all necropsies, and in 10.83% of all cases of cancer coming to necropsy. Cirrhosis of the liver was present in 19 of the cases of primary carcinoma of the liver, whilst the incidence of primary carcinoma of the liver in cirrhosis of the liver was 6.4%.

Cycloserine in tuberculosis.—Varying opinions have been expressed as to the efficacy of cycloserine in the treatment of pulmonary tuberculosis. Bernard and Israel have reported on their results in 31 advanced chronic cases with cavitation which had failed to respond to the 'triple classical treatment'. Cycloserine was given in conjunction with PAS, viomycin or isoniazid, and it is claimed that the simultaneous administration of tranquillizers allowed the drug to be given for several months without any signs of intolerance developing, and with a modicum of success (15 to 20%). Dumon and his colleagues have suggested that the toxic effects would be reduced if the drug were given by aerosol. Other workers are not particularly worried by the toxicity of cycloserine, but consider that the results obtained with its use are scarcely satisfying.

Prolonged pregnancy.—Prolonged pregnancy, which he defines as amenorrhœa exceeding 300 days, occurs in about 5% of all pregnancies, according to Magnin. The lack of knowledge as to its causation he attributes to our ignorance of the factors responsible for the normal onset of labour. On the whole he favours the view that the fault lies in the placenta, but whether this fault is one of delay in 'physiological placental senescence' or some defect of normal œstrogenic function is a matter of conjecture. Diagnosis depends primarily upon a careful history and radiological examination: the presence of a centre of ossification at the upper end of the humerus is said to be a useful sign of post-maturity. The major danger is in the size of the fœtus: 5.45% of the infant mortality in cases in which pregnancy has exceeded 310 days is due to malformation of the fœtus (usually of the nervous system), asphyxia due to aspiration, hæmorrhage due to trauma during birth, or neonatal respiratory infection. It is therefore recommended that labour should be induced by simple mechanical methods, careful administration of oxytocics, or by Cæsarean section if necessary.

Allergic diseases.—As a result of their experience in 11 cases, P. and S. Blamoutier recommend bleeding for the treatment of acute urticaria and acute angioneurotic œdema. To be effective this bleeding must be prompt and quick: 400 ml. of blood must be removed within five minutes: 'half-measures' are of no avail. They claim that this somewhat drastic treatment results in almost immediate relief of the œdema of the lips and eyelids and the pruritus, and that relief of other symptoms due to visceral œdema, whether of the stomach, intestine, or central nervous system, follows soon afterwards.

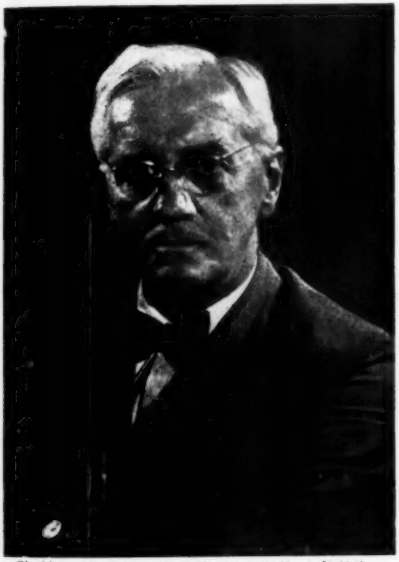
THE PRACTITIONER

Fifty Years Ago

'How the gods must have chuckled when they added Hope to the evils with which they filled Pandora's box, for they knew very well that this was the cruellest evil of them all, since it is Hope that lures mankind to endure its misery to the end'.—W. Somerset Maugham: *A Writer's Notebook*. 1949.

MAY 1908

'OUR readers may or may not be aware that our offices [149 The Strand] and stockrooms suffered, some time ago, from an incursion of what the old-fashioned reporters used to call "the devouring element"—fire. We were obliged, in consequence, to seek temporary premises elsewhere, and make provisional arrangements for continuing business from very cramped and inconvenient headquarters. In



Sir Alexander Fleming, M.D., F.R.C.P., F.R.C.S., F.R.S. (1881-1955)

France they say "it is only the provisional that lasts"; but this is not to be the case with us. We are happy to be able to announce that we have secured new premises, and shall take possession of the whole building as soon as the workmen have taken their departure. Further details will be shortly announced'.

The entire issue of *The Practitioner* fifty years ago is devoted to the 'Opsonic Method' and vaccine therapy in various diseases. This was a subject very near to the heart of W. C. Bosanquet, D.M., F.R.C.P., who was editor from 1902 to 1904 and in 1904 wrote with J. W. H. Eyre for Cassell's 'Modern Methods of Treatment' series the volume on *Serums, Vaccines and Toxins in Treatment and Diagnosis*. According to 'Notes by the Way', 'The method is a new and complex one, and, until its use has been more thoroughly explored, it should only be carried out under the guidance of an expert. In the enthusiasm begotten of the introduction of a new process, there is always the possibility of too much being attempted, and, if practitioners in general act on the notion that they have only to obtain so many millions of bottled bacteria and to inject them into their patients, the process is doomed, and we shall have another fiasco similar to that which followed the first introduction of tuberculin. . . . Whether an opsonic control of the injections will always be necessary still remains to be shown, but for a long time yet the exhibition of the vaccines should be preceded by a most careful bacteriological examination, and, if possible, the particular vaccine should be prepared for each individual patient. If these precautions are taken, there is little doubt that the opsonic method, and vaccine-therapy, has a brilliant future before it; at present, however, it is certainly in the experimental stage, and should be so regarded'.

Sir Almroth Wright, who in the first few years of the present century introduced general vaccine therapy through his work on typhoid inoculation and who in 1903 measured the protective substances in the blood by means of the opsonic index, contributes the opening article, 'On Some Points in Connection with Vaccine-Therapy and Therapeutic Immunisation Generally': 42 pages in length, this must be one of the longest articles ever published in *The Practitioner*.

Alexander Fleming, L.R.C.P., M.R.C.S. Eng. (from the Laboratory of the Inoculation Department, St. Mary's Hospital) makes 'Some Observations on the Opsonic Index, with Special Reference to the Accuracy of the Method, and to Some of the Sources of Error'. Alexander Fleming became a student at St. Mary's Hospital Medical School in 1901, took the Conjoint qualification in 1906, and the M.B., B.S.

London in 1908 with honours in five subjects and a gold medal, and in 1909 passed the F.R.C.S. Immediately after qualifying he started working with Almroth Wright as assistant bacteriologist. He was appointed lecturer in bacteriology in 1920, professor in 1928, and emeritus professor in 1948. From 1946 till 1954 he was principal of the Wright-Fleming Institute of Microbiology. He became world-famous as the discoverer of penicillin and was awarded the Nobel Prize for Medicine in 1945. According to the bibliography appended to Fleming's obituary by Leonard Colebrook (*Biographical Memoirs of Fellows of The Royal Society*, 1956), the article in *The Practitioner* was his second publication. R. Cruickshank (*J. Path. Bact.*, 1956, **72,** 698) comments on this paper's 'original observations on auto-agglutination of red blood cells in infective conditions, which perhaps heralded the much later discovery of the rapid erythrocyte sedimentation rate associated with infection'.

Arthur H. White, Professor of Pathology, Royal College of Surgeons in Ireland, describes 'The Experimental Error in the Method of Determining the Tuberculo-opsonic Index of the Blood'; M. Greenwood, Jr., M.R.C.S., L.R.C.P., Director of the London Hospital Statistical Department and Senior Demonstrator of Physiology in the Medical College, deals with 'Statistical Considerations Relative to the Opsonic Index'; A. C. Inman of the Brompton Hospital discusses 'The Value of the Opsonic Index in the Treatment of Pulmonary Tuberculosis'; and J. Charlton Briscoe, M.D., M.R.C.P., and E. U. Williams, M.R.C.S., L.R.C.P., write on 'The Treatment of Pulmonary Affections by the Inoculation of Vaccines Controlled by the Opsonic Index'.

H. Stansfield Collier, F.R.C.S., of St. Mary's Hospital, in 'A Surgical View of the Opsonic Method', relates that 'In the early days of the opsonic theory, I was strongly, and not altogether pleasurably, attracted to it by the results of its application to some of my cases . . . I consider the opsonic index extremely valuable in guiding one to the indications for employing a vaccine, in gauging the dose, and repeating it at suitable intervals . . . to do the best for our patients, we must be clinically associated with the opsonists'. Other articles are concerned with the value of the opsonic method in skin diseases (Arthur Whitfield), in ulcerative endocarditis (Thomas Horder), in tuberculosis of the genito-urinary organs (J. W. Thomson Walker), and in diseases of the eye (R. W. Allen). W. R. B.

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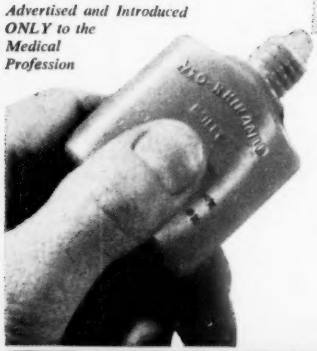

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